A STUDY OF NEUROLOGICAL SOFT SIGNS IN POSITIVE AND NEGATIVE SUBTYPE OF SCHIZOPHRENIA

DISSERTATION SUBMITTED FOR PARTIAL FULFILLMENT

OF THE RULES AND REGULATIONS

DOCTOR OF MEDICINE

BRANCH - XVIII (PSYCHIATRY)

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY,

CHENNAI, TAMIL NADU.

APRIL 2015

CERTIFICATE

This is to certify that this dissertation titled **"A STUDY OF NEUROLOGICAL SOFT SIGNS IN POSITIVE AND NEGATIVE SUBTYPE OF SCHIZOPHRENIA'' INSTITUTE OF MENTAL HEALTH, MADRAS MEDICAL COLLEGE** submitted by **Dr. C. KAVITHA**, appearing for **M.D (Psychiatry)** degree examination in April 2015 is a original bona fide Record of work done from 2015 by her under my guidance and supervision in part fulfillment of requirements of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

The Director,
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The Dean,
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CERTIFICATE OF GUIDE

"A STUDY OF NEUROLOGICAL SOFT SIGNS IN POSITIVE AND NEGATIVE SUBTYPE OF SCHIZOPHRENIA'' INSTITUTE OF MENTAL HEALTH, MADRAS MEDICAL COLLEGE is the original work of Dr. C. KAVITHA, done under my guidance submitted in partial fulfilment of the requirements for M.D. Branch – XVIII [Psychiatry] examination of The Tamilnadu Dr. M. G. R. Medical University, to be held in April 2015.

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DECLARATION

I, **Dr. C. KAVITHA,** solemnly declare that this dissertation **"A STUDY OF NEUROLOGICAL SOFT SIGNS IN POSITIVE AND NEGATIVE SUBTYPE OF SCHIZOPHRENIA''** was done by me at the, Institute of Mental Health, Chennai under the guidance and supervision of **Dr. JEYAPRAKASH R.** MD, DPM, the Professor of Psychiatry, Institute of Mental Health , Madras Medical College.

This dissertation is submitted to the Tamil Nadu Dr .M.G.R. Medical University, Chennai – 32 in partial fulfillment of the University requirements for the award of the degree of M.D., Psychiatry.

Place: Chennai

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(C. KAVITHA)

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I dedicate this thesis to my teachers and my family.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

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To
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Dear Dr. C.Kavitha,

The Institutional Ethics Committee has considered your request and approved your study titled **"A study of neurological soft signs in positive and negative sub types schizophrenia" No.10082014.**

The following members of Ethics Committee were present in the meeting held on 05.08.2014 conducted at Madras Medical College, Chennai-3.

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We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

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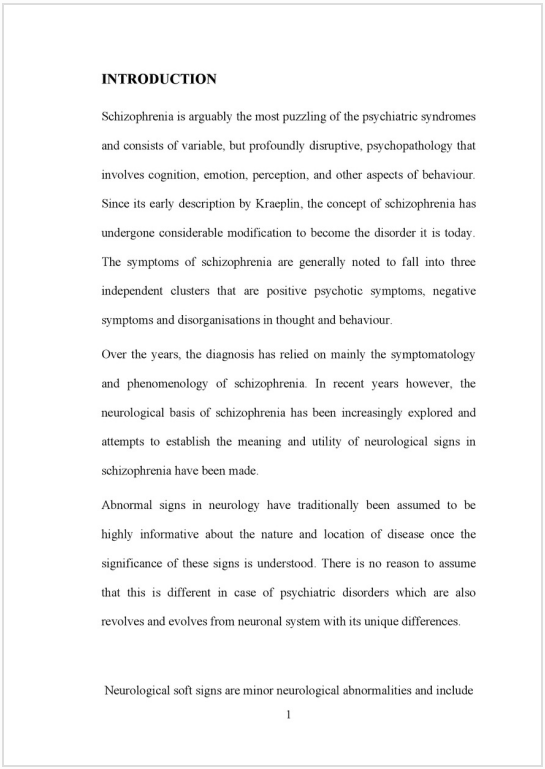

INTRODUCTION

Schizophrenia is arguably the most puzzling of the psychiatric syndromes and consists of variable, but profoundly disruptive, psychopathology that involves cognition, emotion, perception, and other aspects of behaviour. Since its early description by Kraeplin, the concept of schizophrenia has undergone considerable modification to become the disorder it is today. The symptoms of schizophrenia are generally noted to fall into three independent clusters that are positive psychotic symptoms, negative symptoms and disorganisations in thought and behaviour.

Over the years, the diagnosis has relied on mainly the symptomatology and phenomenology of schizophrenia. In recent years however, the neurological basis of schizophrenia has been increasingly explored and attempts to establish the meaning and utility of neurological signs in schizophrenia have been made.

Abnormal signs in neurology have traditionally been assumed to be highly informative about the nature and location of disease once the significance of these signs is understood. There is no reason to assume that this is different in case of psychiatric disorders which are also revolves and evolves from neuronal system with its unique differences.

Neurological soft signs are minor neurological abnormalities and include

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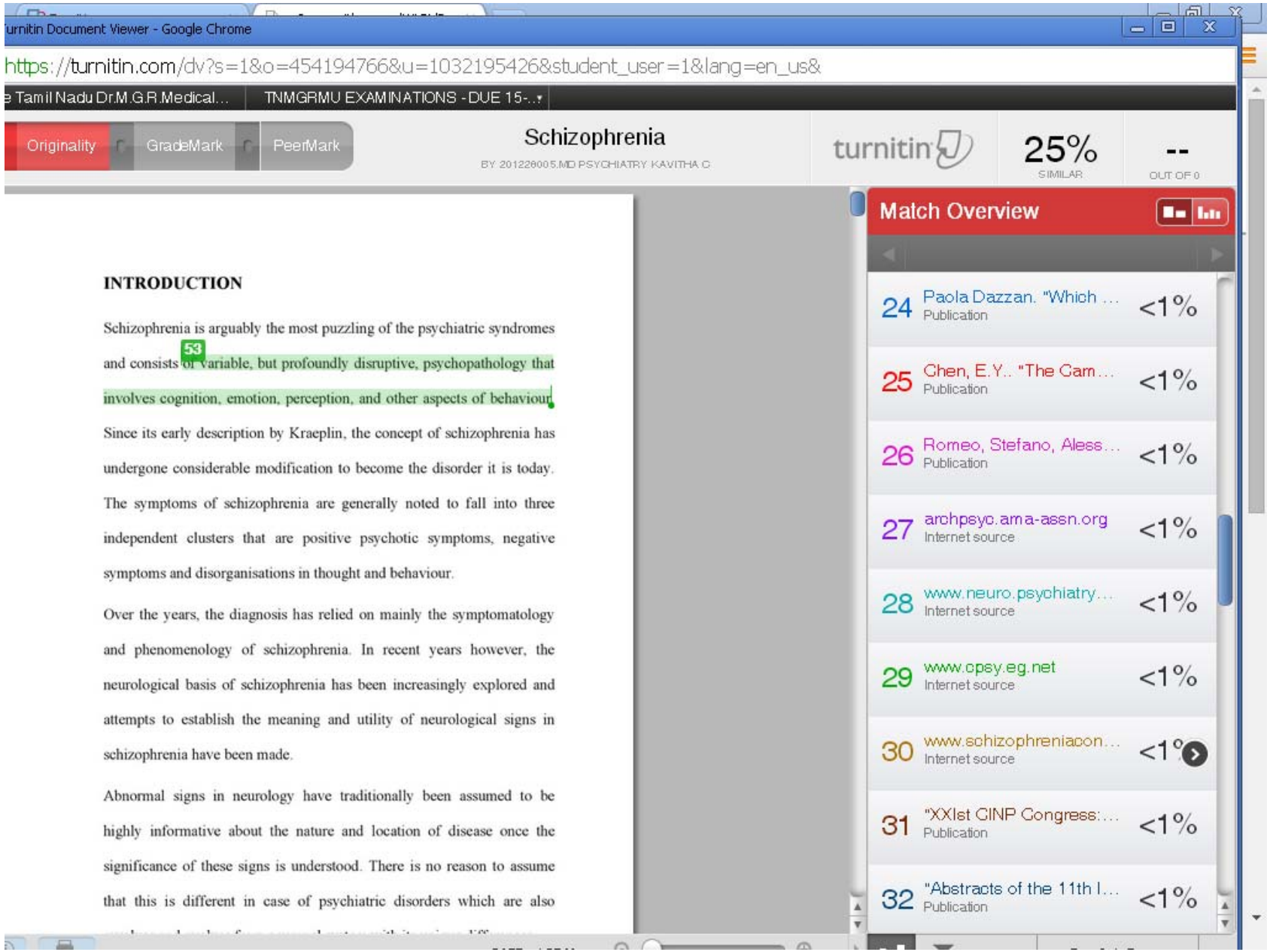
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CONTENTS

"A STUDY OF NEUROLOGICAL SOFT SIGN IN POSITIVE AND NEGATIVE SUBTYPE OF SCHIZOPHRENIA''

ABSTRACT

Background and Objectives

Soft neurological signs have been observed in patients with schizophrenia. There are several studies demonstrating neurological impairments in schizophrenia patients but their presence has been complicated by a number of potentially confounding variables such as the duration of the illness, medication doses and the use of different measurement techniques. Soft neurological signs appear to be a trait feature of schizophrenia as well as a possible biological marker of its prognosis.

Therefore, their early detection and the consequent early intervention may lead to a better prognosis. Assessment of the soft neurological signs is a direct, easily administered and inexpensive way of investigating the severity of brain dysfunction in schizophrenia. The co-relation between the positive and negative subtype of schizophrenia and soft neurological signs in a patient has not been extensively studied in the context of the Indian population. Therefore, this study aims to evaluate the presence of soft neurological signs in patients diagnosed with schizophrenia.

Method

Sixty subjects, 30 patients with Positive schizophrenia and 30 patients with Negative schizophrenia were evaluated. Tools used were PANSS for evaluation of symptomatology in schizophrenia patients, NES for evaluation of neurological soft signs, Self structured proforma for assessing socio demographic status.

Statistics used: Students t test χ^2 (Chi-square), Binary Logistic Regression, with the help of the statistical package namely IBM SPSS Statistics-20.

Results

Socio-demographic variables and clinical variables like age gender, educational status, duration of illness have no correlation with presence of soft neurological signs in patients with schizophrenia. Statistically there is no significant positive correlations are observed between the negative and positive symptom subscale of PANSS and the NES scores.

Among the NES Subscales, sensory integration and Others items in NES score are Statistically significantly positive in negative type of schizophrenic patients schizophrenia.

Conclusions

Soft neurological signs are observed in adult patients with schizophrenia and the presence of these signs are not correlated with both positive and negative syndrome of schizophrenia

Key Words: Schizophrenia, Soft neurological signs.NES

INTRODUCTION

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Neurological soft signs are minor neurological abnormalities and include impairments in functions such as sensory integration, motor co-ordination and the sequencing of complex motor acts.

Neurological signs are traditionally classified in to Hard and Soft signs. Neurological signs are traditionally classified in to Hard and Soft signs. ‘Soft signs’ are not readily localisable to specific brain regions and are assumed to indicate a diffuse brain dysfunction, between cortical-subcortical and inter cortical areas. In contrast ‘hard signs’ which are neurological signs localisable to specific brain regions,indicates neuro anatomical damage (**BARKUS et al 2006).**

Buchanan and Hein richs classified a NSS into three domains based on neuro anatomy and function. They are integrative sensory function (dysfunction of the hetero modal cortex), motor coordination (basal ganglia abnormalities), sequencing complex motor acts (deficit of fronto -basal ganglia circuitry)

Several studies have consistently demonstrated the presence of soft neurological signs in schizophrenia to a greater extent as compared to other psychiatric disorders. Classic descriptions of the psychiatric disorders often included neurological exam findings. Thus, “insane temperament’’, “hysteria’’ schizophrenia, mood disorders and obsessive-

compulsive disorders were each thought to have characteristic neurologic exam abnormalities (Sanders & keshavan, 1998).

The clinical significance of these signs in schizophrenia is as yet poorly understood. It is postulated that soft signs may be a non-specific marker of a patient's vulnerability to psychosis or that they could modify the clinical manifestations and course of schizophrenia. In the light of cerebellar function abnormalities demonstrated in schizophrenia patients, it could be an indicator of the underlying cerebellar dysfunction in schizophrenia patients. It could also be of etiological significance pointing to a distinct sub-type of the disorder. Alternatively, these signs could be related to the cognitive impairments seen in schizophrenia patients.

Factors relating to the patient such as age, sex, period of the illness, level of education may have a relationship with the observed neurological deficits. The severity of the illness and the predominance of a particular symptoms cluster in the patient may also impact the development of soft neurological signs.

Manschreck TC, 198 Studies have demonstrated that negative symptoms may have some structural background and this may be manifest by the presence of soft signs. A strong association has also been

found between formal thought disorder in schizophrenia and soft neurological signs.

As a whole that soft neurological signs have been found to be more strongly related to the presence of schizophrenia, than hard signs. **(BOMBIN et al 2005).**

The prevalence rates of neurological signs in patients with schizophrenia ranges from 50-65% and 5% in normal controls.

Also studies with first episode patients, with out drugs had more soft signs score than before starting medication, thus supporting the notion that they are an intrinsic feature of schizophrenia and strengthening the neurodevelopmental etio pathogenesis of schizophrenia.

Johannes Schröder, MD et al 2008

He had declared that Neurological soft signs denotes the disease activity and these signs vary with psychopathological symptoms through out the disease process, as these signs deflect the disease activity and not a stable feature, so these signs can be considered as clinical predictor of outcome in the future with more research going on this area.

The study of the neurological dysfunction of schizophrenia involves various neuroradiological, neuroanatomical, neuropathological and neuropsychological tests.

The study of neurological soft signs is a simple, inexpensive and direct method of investigating the severity of impairment. Positive correlations if identified may be applicable in a variety of clinical settings including the diagnosis or prognosis of schizophrenia.

This study was undertaken with a view to study the presence of NSS in patients with first episode schizophrenia, to assess the soft neurological sign in positive and negative subtype, and understand their relationship with socio- demographic factors.

NEED FOR THE STUDY

Schizophrenia is a loose and complex neuropsychiatric syndrome Characterised by a range of cognitive and psycho physiological impairment.

Neurological soft signs are subtle non-localizing neurological impairments including of defect in sensory integration, motor co-ordination with inhibition.

The presence of neurological soft signs in schizophrenia patients had been intricated by some hidden issues such as the duration of the

illness, medication doses and the use of different measurement techniques.

However, though neuroleptic medications may have an impact on the severity of these signs, their presence in anti-psychotic naïve patients, suggest them to be a fundamental characteristic of schizophrenia.

Soft neurological signs seem to be a trait feature of schizophrenia as well as a possible biological marker of its out come. Therefore, it will be diagnosed quickly and the consequent early intervention may lead to a good prognosis.

Also in the form of a higher association of neurological soft signs in the subjects of schizophrenia as compared with other mental illnesses, they may be used to identify patients who are more prone to develope schizophrenia.

Assessment of the soft neurological signs will be given easily and inexpensive way of examining the severity of brain dysfunction in schizophrenia and which is quiet straight.

The correlation between the presence of schizophrenia and soft neurological signs in a patient has not been extensively studied in the context of the Indian population.

Therefore, our aim is to compare soft neurological signs in patients diagnosed with schizophrenic subtypes

REVIEW OF LITERATURE

Historical Overview:

In olden years, deviant behavior was attributed to magic and religious ideas of harm forces that entered and occupied a human body. The ignorance and fear associated with these behaviors resulted in the unfortunate victims being subject to procedures such as trephination and burning to free the evil forces. Despite these common religious and spiritual views of mental illness, we should also account scientific theory, and medical hypotheses

Hippocrates and Galen reported deviant behavior and madness which are related to inner imbalances in the body. In the 18th century**,** **Philippe Pinel**, a French physician, claimed that psychiatric illness were a disease of the central nervous system and one that could be caused by familial or environmental factors. He instituted humane techniques to handle psychiatric patients and categorized mental illness into subgroups and identified patients who had disturbances of intelligence, emotion, or desire. These olden concepts made easy to our 21st century conceptualization of schizophrenia. Our modern understanding of schizophrenia can begin with a look back to the19th century.

DURIG 1828-1896 reported that schizophrenic patients had disturbances of action are high at the level of motivation or will than at the level of need .

Reynolds & Jackson (1834-1911) they originally described distinction between positive and negative patients. Positive symptoms can occur due to overstatement of normal brain process, where as negative symptoms were conceptualizes as a diminution or negation of normal process.

Emil Kraepelin (1856–1926) a German psychiatrist was one of the first to distinguish manic-depressive psychoses from other chronic psychotic illnesses. He published a detailed account of his patients' symptoms in a monograph entitled Dementia Praecox and Paraphrenia.

Eugene Bleuler (1857- 1939) was a Swiss psychiatrist who coined the word schizophrenia. In his literature entitled "Dementia praecox and the group of schizophrenias," he put forth his theory that schizophrenia consisted of not just one illness with one etiological basis but a heterogeneous group of illnesses with distinguishing characteristics and clinical courses (Bleuler and Zinkin 1950). He differed from Kraepelin in believing that these illnesses were not as often characterized by an early onset and a terminal dementia.

Bleuler's "four A' s consisted of primary symptoms:

- Ambivalence,
- Loosening of associations,
- Abnormal affect (either excitation or withdrawal), and
- Autistic behavior, which he described as people are living in an internal, unrealistic world, had active social avoidence.

Kurt Schneider (1887–1967) had imbedded the ideas of both kraeplin and bleuler, he had through his vast clinical experience in germany, identified the diagnostic symptoms of schizophrenia

Strauss et al (1974); had contributed to the symptoms types of psychopathological manifestations; positive symptoms, negative symptoms and disorders of relating.

NancyAndreasen and Olsen (1982); conceptualized positive and negative symptoms as different ends of the same continuum and described patients as either predominantly positive (or)negative symptoms. Subsequently introducing a third mixed group.

T.J .Crow (1985); described the concept of syndromes in schizophrenia,

In type 2 syndrome, so called irreversible part of the pathology correlates more with negative symptoms and type 1, being the reversible phase of the disease – associated with morphological changes in imaging of the

brain. Behavioral abnormalities and cognitive problems are linked with type.

Even after years of research, still the diagnostic criteria is being questioned and debated throughout the world, the etiology of schizophrenia is still puzzling from the years of Eugene Bleuler and Emil Kraepelin,, the pioneers who coined “dementia praecox” .They proposed that abnormalities in the brain – structural and functional changes would be linked to the etiology of schizophrenia. The genetic research in schizophrenia had shown remarkable progress in the etiology of schizophrenia,the most crucial risk factor for schizophrenia is having a strong family history, but a interesting fact is that the chance for a monozygotic twin of a schizophrenic patient to develop the disease is only 48 percent this proves that certain other theories are involved in the etiology - this being neurodevelopmental hypothesis.

Neurodevelopmental hypothesis :

Alterations in the early brain development from utero could be the reason for the occurrence of childhood onset schizophrenia, minimal alterations in ectodermal devolpment, like cranio facial abnormalities could be the reason for adolescent onset of schizophrenia lot of embryological studies show that decreased size of neurons, decreased neuronal density in the hippocampus are postulated behind adolescent

onset Also it has been postulated that defects in synaptic pruning analogous to the programmed elimination of neural elements during very early development may underlie the cases of schizophrenia that emerge during adolescence.

Summarizing the theories

1. The basic problem being a defect or anomaly in early brain development
2. The risk factor, culprit of the pathology is of short duration, and this process is static.
3. There is a quiet period (latency part) between the exposure to the causative factor and the onset of symptoms.

Other catalyst being environmental risk factors and genetic risk factors which stimulates the process to develop in to a full blown disease

Delayed milestones, poor communication with peers, and improper social habits are some of the peadiatric abnormalities supporting this hypothesis

The problem with the neuro developmental hypothesis of schizophrenia is how to explain the long lag between prenatal damage to the foetal brain and the onset of psychotic symptoms in adolescence and early adulthood.

Two models have been proposed to explain this latent period: **1. The early neurodevelopmental model;** This is based on the view that a fixed lesion from early life interacts with normal neurodevelopment occurring later, lying dormant until the brain matures sufficiently to call into operation the damaged systems.

2**. The late neurodevelopmental model.**

Based on data that indicate substantial changes in brain biology during adolescence, this model proposes that schizophrenia may result from an abnormality in peri-adolescent synaptic pruning. 5 Synapse density appears to show a rapid rise following birth until a peak at about two years. This is followed by a decline until a plateau is reached during the late teens. The age at which this plateau is reached is close to the greatest acceleration in onset of schizophrenia. A minimum threshold of use exists below which a synapse is pruned. Early developmental injury could cause 'dyspruning' leading to reduced connectivity and negative symptoms. Compensatory retention or proliferation of some other connections and their anomalous persistence of these circuits could lead to 'parasitic foci' that become autonomous, causing positive symptoms. Thus, the neuro developmental theory, occurring on a background of genetic vulnerability, allows the maximal integration of the

epiphenomena and epidemiological evidence associated with schizophrenia.

Positive symptoms;

Positive symptoms and expressive symptamology refers to those psychopathological process that appear to be exaggerations or disinhibition of normal process.

Hallucinations, Delusions, pressured speech and excessive or painful affect would be examples of positive symptoms.

Hallucination, Delusion are often found in single factor. Thought disorder and bizarre behavior considers as a third factor. The most evident manifestations of schizophrenia, that demarcate the psychotic process, are the positive symptoms and have till recently been the focus of diagnostic and treatment considerations.

However it has been well established that within psychotic illness, positive symptomology has limited prognostic significance.

Negative symptoms and definition;

National Institutes of Mental Health (NIMH), suggested there are five general categories of negative symptoms. The most common negative symptoms are avolition and anhedonia. Negative symptoms do not occur only in schizophrenia, or only in psychiatric illness also

presented in 5 to 10 percent of other disorder. There is a weak but consistent relationship between levels of negative symptoms and levels of disorganization symptoms in populations. They have an increase in familial risk that is not seen for psychotic symptoms, and also greater concordance in monozygotic twins for negative versus psychotic symptoms .Negative symptoms have also been found to consistently correlate with measures of neuropathology, especially those measures of frontal lobe function or the volume of cerebral tissue.

Anhedonia ; is a loss of the ability to find or derive pleasure from activities or relationships and may be the most persistent of the negative symptoms.

Avolition; is the loss of will or drive, in neurology, this is sometimes referred to as abulia. **Affective blunting**; consisting of both an inability to understand or recognize displays of emotion from others and an inability to express emotion, is an important predictor of functional impairment in schizophrenia. Also deficits in production, facial expression, gestures, and prosody, and understanding these social signals.

Social withdrawal; is sometimes referred to as "passive or apathetic social withdrawal" and includes indifference to social relationships and decreases in the drive to socialize. It indicates defect in theory of mind

Alogia is a decrease in verbal communication, and it is found in up to 25 percent of people with schizophrenia. Although alogia has been considered both the loss of production and a deficit of content with a normal volume of words, only the loss of production is a negative symptom.

Affective blunting and alogia, two measures of communication, and social withdrawal are more correlated with each other than they are with anhedonia and avolition, and so it appears there are two general groups of negative symptoms. Poor attention had been considered a negative symptom, but it also appears to be more related to disorganization symptoms than other negative symptoms.

Most commonly used scales for the positive and negative symptoms

SANS (1983 Nancy Andresen) –scales for assessment of negative symptoms

SAPS--- scales for assessment of positive symptoms

PANSS (KAY et al1987)—positive and negative symptoms scale

NSA (Alphs etal 1989)---negative symptoms assessment

SDS (Kirkpatrick et al 1989)—the schedule for the deficit syndrome.

Brief psychiatric rating scales.

PYRATS-- The Psychotic Symptom Rating Scales (PSYRATS) is an instrument designed to quantify the severity of delusions and hallucinations and is typically used in research studies and clinical settings focusing on people with psychosis and schizophrenia..

Neurological signs in psychiatry:

A neurological sign is any objective evidence or manifestation of an illness or disordered function of the body. Signs are more definitive and obvious in contrast to symptoms which are more subjective. A neurological sign may be associated structurally and functionally with a central nervous system deficit. These are called ‘hard signs’ and include hemiplegia, abnormal reflexes, dysarthria sensory abnormalities etc.

Neurological signs may also be ‘soft signs’ which are any neurological deviation motor, sensory or integrative that does not localise to a particular central nervous system site and these may be chronic, non-life-threatening and of unknown aetiology. However, both these types of signs may co-exist in a patient.

Neurological examination in psychiatry serves two main purposes:

- It identifies neurological lesions as the cause of behavioural abnormalities or screen for neurological dysfunction, and

- It evaluates subtle deficits in neurological performance in patients without identifiable neurological disease

Neurological soft signs and their origin

From the time of kraeplin (1919), the association between schizophrenia and neurological abnormalities had been observed .he had described symptoms and signs like headache, convulsions, pupil reactivity, reflex disorders, among these patients. Soft neurological signs represent a connection disorder between subcortical and cortical regions or between cortical regions.

Focal or classical neurological signs denotes localized brain dysfunction where as soft signs are characterized by motor, sensory, integrative functional disorders (woods et al.1987). Lot of studies show that soft neurological signs denotes a disordered 1) motor coordination (Ismail et al 1988), 2) sensorial integration (Quitkin et al 1976) 3) sequencing of complex motor acts (Hein Richs & Buchnan 1988)

Motor coordination disorder is demonstrated by test like opposition index finger thumb test, tandem walk, dysdiadocokinesia, finger nose test. Sequencing of complex motor acts is denoted by fist-edge-palm test, positive ozeretski sign and fist –ring test. Sensory integration disorder reflected through audio-visual integration, graphasthesia, stereognosis, bilateral extinction.

Classification of soft signs:

Rutter, Graham and Yule in 1970 proposed the following classification:

1. Signs that indicate developmental delay and disappear with age:

- Associated/ mirror movements
- Immature grasp
- Difficulty in building blocks
- Lateness in developmental milestones
- Lateness in supporting primitive signs
- Motor awkwardness
- Motor impersistence
- Poor gait, posture, stance
- Opposing fingers to thumb
- Tapping
- Speech articulation problems
- Tactile extinction or double simultaneous stimulation

2. Signs that are unusual findings of clinical neurological examination:

- Astereognosis
- Asymmetries of associated movements
- Audio-visual integration difficulties
- Chorieform movements
- Dysarthria
- Dysgraphaesthesia
- Hypokinesia
- Labile affect
- Motor impersistence
- Nystagmus
- Oromotor apraxia
- Posturing of hands while walking
- Reflex asymmetries
- Significant in coordination
- Increased/ decreased tone
- Tremors
- Word finding difficulties

Shaffer et al in 1985 showed that the prior studies on soft neurological signs have been criticised owing to the following reasons:

1. Misclassification of phenomena due to poor inter-rater agreement
2. Misclassification due to fluctuating states in the subject
3. Signs of focal neuropathology misinterpreted as soft signs
4. Impaired cognitive ability leading to poor neurological performance
5. Multiple statistical comparisons
6. Selection bias
7. Examiner bias

Over the last few years researchers have used many different signs while assessing the soft neurological signs in patients. Bombin et al in their review of literature pertaining to these signs have given the following summary of neurological signs most frequently included in the studies, grouped according to the cluster they belong to and their putative localisation BOX 1 Clusters of soft neurological signs, their localisations and individual signs:

Cluster of Neurological Sign Denomination	Putative Localization	Individual Signs Assessed
Integrative sensory function	Parietal lobe	• Bilateral extinction
		• Audiovisual integration
		• Graph aesthesia
		• Stereo gnosis
		• Right–left confusion
		• Extinction
Motor coordination	Frontal lobe Cerebellar	• Intention tremor
		• Balance
		• Gait
		• Hopping
		• Finger–thumb opposition
		• Dys diadochokinesis
		• Finger-to-nose test
Sequencing of complex motor acts	Prefrontal lobe	• Fist-edge-palm test
		• Fist-ring test
		• Ozeretski test
		• Go/no-go test
		• Rhythm tapping (foot or hand)
Primitive reflexes	Frontal	• Glabellar tap
		• Jaw jerk

		• palmo mental
		• Corneomandibular
		• Pout/snout
		• Sucking/oral
		• Grasp
		• Forced groping
Hard neurological signs	Central nervous system including cranial nerves	• Mirror movements
		• Synkinesis
		• Convergence
		• Gaze impersistence
• Extra pyramidal signs		
• Pyramidal signs		
• Dyskinesia		
• Language		
• Speech		

Differences in Definition

The term soft signs was introduced by **Bender in 1947** to describe findings, suggesting possible neurological disease in his study upon child hood schizophrenia (Sanders & Keshvan, 1998).

Quitkin et al 1976 referred the term soft signs to any neurologic deviation, motor, sensory, or integrative, that does not localize the site of a putative CNS lesion.

David Shaffer et al 1984 said that the designation' soft' is usually taken to indicate that the subjects with signs reflects patients do not have any other static or transient neurological disease .

Woods, Griffths et al 1986, 1998; differentiates the hard and soft by the presence &absence of primary tract or nucleus pathology.

In 1988 in their review, **Heinrichs &Buchanan** ascribes specific functional domains and argues against the notion that the soft signs are nonspecific, and have used the term 'Neurological signs 'throughout their review and named their scale also as a structured instrument for the assessment of 'Neurological signs' in schizophrenia which has signs that are designated as 'soft' elsewhere in the literature.

In 1998 **Griffiths et al** divides neurological signs in to primary and integrative signs with a tendency to reflect focal and diffuse abnormality instead of hard or soft signs and have denied usage of the term soft signs in their study.

In 1998 Sanders & Keshavan suggests the term' Neurologic exam abnormalities' (NEA) instead of hard or soft due to their misleading meaning.

Walter fang et al 2005; Even within the existing scales, the classification each neurological sign as hard or soft (primary or integrative) is very difficult. For example, tests such as the fist–edge–palm test, or the fist ring test, require integration between the sensory and motor systems (integrative signs), but are also indicative of frontal lobe damage (primary signs). The tandem walk or finger–nose tests, which are impaired in sensory motor integration, and also indicates focal cerebellar damage. Finally, cortical release signs (primitive reflexes such as the glabellar, grasp and palmo mental reflexes) appear as a consequence both of frontal lesions and of more diffuse pathology, and therefore cannot be exclusively classified as hard or soft.

Despite these evolving controversies over its definition and usage, the term' Neurological soft signs' is still retained and used in many recent literature and articles eg.Goswami et at 2006, Barkus et al 2006. In addition it has been reiterated that soft neurological signs are more prominent in schizophrenia than hard neurological signs (Bombin et al 2005).

Common validated schedules for assessing neurological abnormalities:

Scale	Areas measured	Rating used
Neurological Evaluation Scale (Buchanan 1989)	Sensory integration, motor coordination, sequencing of motor acts, 'others' (e.g. memory, grasp, gaze, mirror movements)	3-point scale: 0=absent, 1=mild but definite, 2=marked impairment
Cambridge Neurological Inventory (Chen 1995)	Speech, eye movements, selective examination of cranial nerves, extremity examination, soft signs, 'others' (e.g. facial dyskinesia, stereotypy, arm drift/dropping)	4-point scale: 0=normal response, 0.5=equivocal response, 1=abnormal response, 2=grossly abnormal response
Heidelberg Scale (Schroder 1991)	Neurological signs (e.g. station and gait, tandem walking, dysdiadochokinesia, grap aesthesia)	4-point scale: 0=absent, 1=mild, 2=present, 3=marked
Condensed Neurological Examination (Rossi 1990)	Neurological hard signs (e.g. palmomental test, suck reflex, blunt–sharp discrimination), neurological soft signs (e.g. gaze impersistence, oral apraxia, imaginary acts)	2-point scale: 0=absent, 1=present (unless otherwise stated)

Neurological soft signs as an Endo phenotype: Neurological soft signs as an Endo phenotype

Endo phenotype is characterized by heritable, state independent, associated with illness, co segregated with illness within family, found in more numbers of unaffected relatives in the general population.

To defining the genetic etiology of schizophrenia, there is identification of valid Endo phenotypes are essential. However the conceptualisation of these signs as a trait feature of schizophrenia depends not only on their high prevalence in schizophrenia but also on them being directly related to the disease aetio pathophysiology. The evidence for this however, is currently limited. In light of the fact that NSS appear to be a trait feature of schizophrenia and a possible biological marker of prognosis, their early detection could result in early intervention and, hence, may lead to a better prognosis. NSS maybe used to identify subjects at high risk for developing schizophrenia (e.g., psychotic first-episode patients, relatives of patients with schizophrenia). The low predictive value of NSS however, recommends their use in combination with other risk factors.

Also, neurological signs may represent a valid endophenotype, which could help focus genetic research on the aetio pathogenesis of schizophrenia. In order for them to be adopted as a valid biological

marker for genetic research, the genetic mediation of neurological signs needs to be demonstrated.

Neelam et al investigated whether soft signs met a further criterion for an endopheno type, namely familial association. They hypothesized that if familial association were present then neurological soft signs would be:

(a) More common in first-degree relatives of people with schizophrenia thanin controls; and

(b) More common in people with schizophrenia than in their first-degree relatives.

They reviewed studies that carried out a three-way comparison of levels of soft signs between people with schizophrenia, their first degree relatives, and normal controls. Seven studies with 1553 participants were identified. They found that soft signs were significantly more common in first-degree relatives of people with schizophrenia than in controls. Neurological soft signs were also significantly more common in people with schizophrenia than in their first-degree relatives. Thus, both hypotheses were confirmed, suggesting that the distribution of neurological soft signs in people with schizophrenia and their first-degree relatives is consistent with the endopheno type criterion of familial association.

Chan and Gottesman; provide substantial evidence to support the claims that NSS, motor coordination in particular, meet many of the criteria discussed above to evaluate the suitability of the presence of NSS as an endo phenotype for schizophrenia

Ismail et al-compared patients, and their first degree relatives, and healthy variables for neurological abnormality and obstetrics complication. Found that strong correlation between schizophrenia and their own relatives than control in neurological abnormality, motor function, and maximum O&G complications noted in both parents and their siblings finally concluded that the degree of neurological abnormality may be genetically mediated.

Motor coordination signs and disinhibition were more prominent in siblings of schizophrenic patients than in healthy controls – this was observed by Chen et al, and Motor coordination, EPS, Sensory integration signs were more pronounced in patients with schizophrenia, compared to their siblings.

In a study comparing presumed carriers (patients with symptoms, while parents not affected, with history of schizophrenia in a second relative) and healthy controls made by Gourion et al, presumed carriers scored higher in motor coordination and integration than non presumed carriers

In a study comparing three groups, off springs of affected mothers, healthy mothers, and affective psychosis mother – made by Schubert, he had found that off springs of affected mothers had scored higher in hard signs, soft signs, motor functions and motor coordination.

Most of the twin studies support the genetic etiology eg; Neithammer et al reported high rates of soft signs are noted in schizophrenic and their monozygotic twin than in healthy monozygotic. In contrast to this, few studies from Egan et al, Appels et al, Lawrie et al reported that there is no significant soft signs scores differences in patients, their siblings and healthy controls. With these findings and a replicated finding of lack of association between obstetrics complications and NSS in patients, the authors asserts a genetic origin of NSS.

NEUROLOGICAL SIGNS and SOCIODEMOGRAPHIC VARIABLES

Only one out of 12 studies showed gender -preference female patients with a positive family history showed more soft neurological signs.

Studies proved no correlation between age and severity of neurological dysfunction, but a progressive deterioration found in later stages of life.

Inverse relationship between education levels and neurological impairment is found in 4 studies, but 5 other studies – showed no correlation

Factors like ethnicity and socioeconomic status – not assessed adequately. Buchanan et al.1989 they found Poorer pre morbid adjustment in their study, based on the years of education.

Richard D Sanders et al 2000 they found strong correlation between the cognitive–perceptual factor (memory, audiovisual integration, right–left orientation, face–hand test, rhythm tapping reproduction); and full-scale IQ score.

Raymond c k chan 2010 et al Chronicity-related moderation of the NSS effect, they found no statistically significant difference between first-episode schizophrenia and more chronic patients.

Prevalence of neurological soft signs in schizophrenia and other mental disorders

Most of the studies showed a neurological soft signs are more in patients with schizophrenia than in other disorders like obsessive-compulsive disorder, substance abuse and bipolar disorder, alcohol dependence mood disorders non schizophrenia psychosis and mixed psychiatric diagnosis

Most of the studies reports a prevalence rate of 5% among normal controls and 50-65% in persons with schizophrenia,, the prevalence of NSS among other psychiatric disorders ranges from 5- 50 %

This wide range of prevalence is indeed due to the difference in the definition of neurological impairment.

A very high prevalence rate of 80 -90% is found in studies – which uses only one neurological soft signs at least for diagnosis, where as the prevalence dips to 30-48% in king et al- where he uses 2 or more neurological signs

The total no of neurological signs also ranges in between 4 -104, among these signs - sequencing of complex motor acts and sensory integration are more common among persons with schizophrenia. The parietal area and frontal / prefrontal brain areas are associated with these signs

Bolton et al- concluded more hard signs and motor coordination scores are compared in schizophrenia and persons with obsessive compulsive disorder.

High scores on Cerebellar and cortical sensory neurological signs- showed by Kinney et al, comparing schizophrenia patients with controls and substance abuse bipolar disorders.

Mohr et al in his study, comparing with alcohol dependent patients concluded that non chronic schizophrenic patients scored more on motor coordination sub scale and chronic schizophrenic patients scored more on all sub scales.

In a study – Krebs et al, comparing schizophrenia and mood disorder patients – "motor integration was the most distinctive factor.

In his study Keshavan et al, compared to patients with non schizophrenic psychosis, more of sensory integration and cognitively signs were present in schizophrenia patients, with no significant difference in motor signs**.**

TABLE 2

Functional areas frequently reported as abnormal in schizophrenia and tests that can elicit disturbances in these areas

Functional area	Test
Primitive reflexes	Gaze
	Palmo mental
	Snout
	Grasp
Sensory integration	Audio-visual integration
	Stereo gnosis
	Graph aesthesia
	Extinction
	Right–left confusion
Motor coordination	Tandem walk
	Rapid alternating movements
	Finger–thumb opposition
	Finger–nose
	Rhythm tapping
Motor sequencing	Fist–ring
	Fist–edge–palm
	Oszeretski test

Motor coordination signs have been shown to be specifically associated with impairments in action and attention inhibition (Mohr F et al,Hubmann w etal 1996,2003).

Chen et al;.described a progressive increase over 3 years in these NSS in schizophrenia mainly motor coordination, sensory integration and disinhibition.

Flyckt et al 1999;

Duration of illness, neuroleptic medication and negative symptoms were not related to the occurrence of neurological signs and psychomotor performance. These findings indicate that neurological aberrations are present at the onset of illness and that hereditary factors are associated with motor laterality.

NEUROLOGICAL SOFT SIGN IN FIRST EPISODE SCHIZOPHRENIA:

Patients with specific minimum symptoms in a specified duration, fulfilling the criteria for a psychotic disorder. - Keshavan and Schooler (1992)

Illness onset was defined as - onset of first sign of mental disturbance (nonspecific) by Hafner et al (1993).

Episode onset is defined as the first occurrence of first rank symptoms - (specific).

First episode- Yung et al 1996, defined as patient himself experiencing symptoms for the first time or reported by people near him.

Recent Cross Sectional Studies of NSS in First-episode Schizophrenia

Study	NSS Scales & Psychometric Instruments	Subjects	Results
Bottmer et al.,	Heidelberg	37 psychotic patients (20 schizophrenia, 2 schizoaffective disorder, 14, schizophreniform disorder, 1 psychotic disorder not otherwise specified 18 healthy controls	lower cerebellar volumes found in schizophrenia patients- this finding was associated with higher NSS scores.
Prikryl et al.,	Neurological Evaluation Scale (NES)	88 male patients	Definitive association between negative symptoms and neurological soft signs
Dazzan et al.,	Neurological Evaluation Scale	77 patients with psychotic disorders	Gray matter density-reduced in bilaterally lenticular

			nucleus, right middle temporalgyrus; left middle temporal gyrus,left putamen, right precentral gyrus,and lingual,thalamus gyrus and reduced white matter intensity in leftinternal capsule-
Varambally et al.,	Modified Neurological Evaluation Scale	32 schizophrenics without antipsychotics 30 healthy participants	sensory integration and cerebellar functioning scores were higher in patients with schizophrenia
Poyurovsky et al.,	Neurological Evaluation Scale	59 Schizophrenia Patients (20 first- episode) withobsessive-compulsive disorder. 51 patients with schizophrenia 20 patients without an obsessive-compulsive disorder (OCD) 51 healthy people	No significant difference found in patients with or with out ocd
Zabala et al., (2006)	Neurological Evaluation Scale	8schizophrenic adolescents with, 15 non-schizophrenic	adolescents with psychosis had high score in NES score, when compared to the normal patients

		psychosis 39 normal patients	high scores for schizophrenic psychosis compared to other groups
Thomann et al.,	Heidelberg NSS (MRI) analyzed by voxel based morphometry	42 patients with schizophrenia first episode 22 healthy patients	Healthy patients scored high in soft signs frontal cortex changes were associated with high scores in healthy patients alterations in sensorimotor cortex, cerebellum, thalamus, caudate nucleus – head were linked with patients with first episode

Neurological signs and cognition:

Cognitive impairment is a well- documented phenomenon in schizophrenia

Marder S Retal 2004

Executive functioning a very important part of cognitive capabilities is lost in schizophrenia. Certain factors which contribute to this are – solving problems, attentiveness, reason out capabilities and processing information. So wherever there is neurological damage there is loss of cognition

Mohr et al and smith et al cognitive functioning, which includes executive functions were closely related and merited by sequencing of complex motor functions

Chen et al. has emphasized on cognitive functions and their importance in assessing neurological functions, problems with attentiveness is related only with some soft sign subsclaes, so he had insisted researchers to concentrate on specific cognitive and their correlating signs

Flashman LA, Flaum M, (1996) et al, Jahn T, Hubmann W (, 2006)

Soft signs and neuropsychological deficits in patients with schizophrenia were found to be strongly associated even after medication, extra pyramidal symptoms, and involuntary movements were controlled for, in a study of 176 patients. The deficits were particularly in tasks that assessed motor coordination and timed motor speed.

Dazzan P, Lloyd T et al (2008)

Higher rates of primary and motor coordination signs were not associated with lower cognitive ability and were found to be specific to the presence of psychosis.

Neurological soft sign and brain morphology in first episode schizophrenia:

Brain imaging studies suggests that NSS are partly localizable and may be associated with deficits in specific brain areas.

Recent post-mortem and neuroimaging studies of schizophrenia delineate changes in brain structure and volume that appear to arise from a reduction of neuritic processes (such as dendrites and synapses) rather than loss of neuronal or glial cell bodies. Reduced synaptic connectivity arising from disturbances of brain development active during peri natal and adolescent periods could account for these changes.

Johnstone EC, etal 1976

Initial CT studies using Ventricle Brain Ratio (VBR) reported that patients with schizophrenia had abnormally large ventricles

Keshavan MS, Corson PW, (1998, 1999) --- recent evidence of the caudate nucleus volume being reduced in neuroleptic -naive schizophrenia

Mc Creadie RG, 2002 Untreated patients with schizophrenia having spontaneous dyskinesia had a larger lentiform nucleus as compared to the controls.

Rubin et al. (1994) examined 45 subjects with schizophrenia and 24 healthy people for NSS along with CT scan and regional Cerebral Blood Flow (RCBF). NSS were associated with smaller brain volume.

Oliver gay, Marion plaze 2013

Found that in patients with increased NSS has low global-sulcal index in both hemispheres& decreased regional–sulcal index in Lt DLFC,Rt lateral occipital cortex.

Meta analysis for brain pathology was done byQuing zhao etal 2014 Zhi li etal. They have done 6 structural MRI and 15 FMRI in schizophrenic patients to support the conceptualization of NSS as a manifestation of cerebello thalamo prefrontal brain net work model. Results from SMRI showed NSS were associated with atrophy of the pre central gyrus and cerebellum, inferior frontal gyrus, and the thalamus, and FMRI shows altered brain activation in the inferior frontal gyrus, bilateral putamen, the cerebellum, and the superior temporal gyrus.

Lewis S (1997)

Several studies have failed to find a correlation between the length of illness and degree of volumetric reduction, supporting a developmental etiology for these deficits rather than degenerative.

Positron emission tomography (PET) studies have shown a prefrontal–thalamic–cerebellar network is activated when healthy subjects recalling

complex narrative material, but in subjects with schizophrenia, it is not activated when they are doing the same task.

The positive symptom subscale correlated inversely with gray matter volume (GMV) and cortical thickness in frontal and temporal regions, whereas the negative symptom subscale correlated inversely with right frontal cortical surface area also they found Cortical thickness demonstrated more associations with psychopathology than cortical surface area. (Jeya L Padmanabhan 2014)

Association with antipsychotic medication:

Scheffer and others etal they have studied NSS in 26 schizophreniform psychosis patients with out drugs and 3 drug-free patients by using NES in 6 wks interval and found that there is no significant changes in NES scores.

Marco M.picchioni and paola Dazzan et al

Extrapyramidal side-effects are conceptually distinct from neurological abnormalities, and although a wealth of evidence suggests that the excess of abnormalities is not an epiphenomenon of antipsychotic treatment, the relationship between neurological abnormalities and antipsychotic medication remains contentious.

Several number of studies have found there is noassociations between antipsychotic dosage and overall severity of neurological impairement.

Cerebellar dysfunction in schizophrenia:

Saccadic eyeball movements and disturbed smooth pursuit eye movements have been well described.

Levin S, Holzman PS, 1981 Chaudhury SG 1997 et al

Saccadic Eye Movement (dysfunction measured by instrumentation) was found in 54.6% of the patients with schizophrenia (18/33) as compared with only 6.7% (2/30) of healthy controls. Higher SEM dysfunction is associated with negative symptoms. It has been connected to abnormalities in the anterior vermis of the cerebe llum and the fastigial nucleus.

Kinney DK et al 1999

Signs of cerebellar and cortical sensory dysfunction have been reported to be higher in patients with schizophrenia as well as their first-degree relatives compared to healthy controls

Sears LL et al2000

Patients with schizophrenia were demonstrated to have facilitated eye blink conditioning compared to control subjects, suggesting an

enhanced excitability in the cerebellum as part of a disrupted Cortical-Thalamic-Cerebellar-Cortical Circuit (CCTCC) in schizophrenia

Deshmukh et al. 2002 compared clinical signs of cerebellar dysfunction in 34 subjects with schizophrenia, 15 alcohol dependence 15, and 28 normal controls. Patients with schizophrenia had impaired stance with eyes closed, dysdiadochokinesia and gait abnormalities as compared to controls, and more dys diadochokinesia as compared to patients with alcohol dependence.

De GelderB etal2003 Integration of information provided simultaneously by audition and vision was studied in a group of 18 schizophrenic patients. in the audio-visual speech task, there was an impairment in lip reading as well as a smaller impact of lip reading on auditory speech information, suggest that there is an integration deficit in the schizophrenic group that is related to the processing of phonetic information

Varambally et al 2006

32 never-treated subjects with schizophrenia and age-, sex-, handedness-, and education- compared normal peoples using the modified NES, Cerebellar functioning was assessed with the International Cooperative Ataxia Rating Scale (ICARS), the Abnormal Involuntary Movement Scale (AIMS), The Simpson–Angus Extrapyramidal Side

Effects Scale (SAEPS). They have found that patients had significantly more NSS, cerebellar dysfunction, and extrapyramidal symptomsPatients who had cerebellar dysfunction as indicated by ICARS scores had more negative symptoms. Which indicates neurobehavioral link between the cerebellum and negative syndrome.

Studies in neuroleptic –naïve patients:

Many of the earlier studies showed patient was not under proper screening for alcohol abuse or dependence. This left some doubts as to the attribution of the neurological findings to possible medication or alcohol effects. For clearing this issuses, there was a need to examine patients who were anti psychotic naïve and free from alcohol to establish the presence of NSS in this individual.

Recently many studies are published regarding drug and naïve first episode schizophrenia Gupta S, Andreasen NC, 1995 –compared NSS in first episode neuroleptic naïve and patients on treatment and healthy controls found soft signs in 23% of the drug axim and 46% of the treated patients also correlated with abnormal involuntary movements scale and simpson-angus extrapyramidal symptoms scores

Venkatasubramanian G et al (2003) studied 21 drugnaive patients matched with 21 normal controls using the Modified Neurological Evaluation Scale with good inter-rater reliability .Finally concluded that

NSS scores high in never treated patients and lack of association with illness duration

Gupta et al have found that NSS and developmental reflex were present in antipsychotic naïve patients, a significantly higher proportion than in a normal sample.

V A-Mittal et al (2007), Hasen Kamp w; they have studied 19 un medicated male patients treated with haloperidol for 6wks and assessed NSS in pre and post treatment. Finally concluded that NSS at untreated baseline are associated with baseline symptom severity and high scores indicates predictive of a smaller degree of improvement in after treated patients

Scheffer et al studied 26 drug naive and 3 drug free schizophreni form patients by using NES prior to treatment & after 6wk antipsychotic treatment, and found that no significant changes in NES score

Studies supporting NSS& Positive and Negative symptoms:

E Y Chen at el (1996) studied in 204 Hong hong Chinese patients with schizophrenia for assessing negative symptoms, NSS, and neuropsychological impairements by using High Royds evaluation of negativity scale, NES. They have found that negative symptoms are modestly correlated with dyskinesia and catatonic features .While there is

little relationship with the traditional soft signs, (motor coordination, sensory integration and disinhibition signs)

Merrian A E (1990) they have administered Neurological inventory and PANSS to 28 chronic schizophrenic in patients and controls, concluded that there was no association between any neurological sign and age, extrapyramidal symptoms, general nneuropsychological integrity, education, iq, or severity or chronicity of illness. negative symptoms specically related to prefrontal deficit.

Mahesh Hembram eta l2014 they have found comparision of NSS in patients with positive and negative schizophrenia revealed that the total score of NES was significantly higher in the negative subtype

Tiryaki etal found that the sub score of sequencing of complex motor acts is a significant predictor of deficit state which is the negative subtype of schizophrenia

Tijana Cvetić et al (2009) compared to positive subtype, higher scores on soft neurological signs were associated with negative subtype. He had also observed that patients found difficulty in performing motor coordination and sensory integration. So soft signs do play a significant role in differentiating in schizophrenia – sub types.

Braun CM 1995 had found in their study –that the prevalence of motor soft signs to be higher compared to sensory perceptual signs in

30 patients who were all unemployed. neuro functional imaging also correlated with frontal lobe and a predominance of left hemisphere involvement, the scales used in this research being scale of life-time history of violence, Nathan Kline Institute scale of soft signs, the negative and positive symptom scale (PANSS).

Tosato etal 2005 neurological abnormalities show relatively little relationship to positive psychotic symptoms motor dysfunction high in positive symptoms

Schroder 1991 high neurological abnormality scores associated with disorganization behavior.

Arango et al2000 disorganisation behavior highly specific for sensory integration and the sequencing of complex motor acts

Yazici 2002, Prikryl 2006) neurological abnormalities appears to be strongly correlated with current and future negative symptoms

Wilma G. Rosen 1984 the diagnostic criteria followed in this study were Langfeldt's criteria, the 12-point Flexible sytem, Schneider's first-rank symptoms, RDC . the study was aimed in identifying poor prognostic factors in schizophrenia the results showed no association in negative symptoms and positive symptoms, related to any diagnostic criteria

Radovan prikryl 2012 andreasen remission criteria used in this study.and soft signs were compared with remitters and non remitters. Patients

followed up for 4 years, remitters- 57% of patients and NES scores reduced and NES scores increased in 43% non remitters.

King DJ, Wilson, A, Mohr ETAL

Had observed globally that studies which had a soft sign correlation positive symptoms did correlate with negative symptoms-too resulting in a selection bias to a symptomatic group., so he had confronted that there is no correlation among soft signs and positive symptoms

Schroder et al. and Whitty et al.-higher scores were observed in acutely presenting patients and a remission from this acute period is characterised by lower scores.

Clinical significance of neurological abnormalities in psychosis:

Psychosis encompasses a group of disorders that present with problems in emotion, thought structure, perception, cognition and volition we can start to identify subgroups of patients who are at greatest risk of developing more negative symptoms and cognitive impairment, by assessing the magnitude of neurological abnormalities in patients with psychosis and who will have a poorer functional outcome.

By using this information early on in the course of the illness, we can begin to identify those patients who are most likely to present with

complex medical, cognitive and social care needs, and who are likely to require greater levels of support to maximize their functional recovery.

Can neurological abnormalities predict proneness to psychosis? :

Dazzan .etal 2002

Neurological abnormalities are an intrinsic part of vulnerability to psychosis and that they have presented more in the earliest phases of the disorder

Cannon 2001 et al Impairments of motor development and fine motor coordination have been observed in children who later develop schizophrenia. Suggests that, it is a marker of latent neuro developmental abnormality, itself acting as the foundation for the risk of schizophrenia.

Barkus 2006 etal

- Even though neurological abnormalities correlate with psychosis proneness and schizotypal traits in the general population, they are not yet a sensitive enough tool to discriminate between those who will and will not develop schizophrenia from these high-risk populations .

AIM OF THE STUDY

- To compare soft neurological signs in positive and negative subtypes of schizophrenia.
- And assess the type of soft signs associated with positive and negative symptomatology of schizophrenia

HYPOTHESIS

- The prevalence of Neurological soft signs is higher in first episode schizophrenia.
- And there is strong association between NSS and Negative symptoms of schizophrenia.

MATERIALS AND METHODS

DESIGN OF THE STUDY;

- Cross sectional analytical study

Setting

This study was carried out on the patients who attended OPD and who were admitted in ward in Institute of mental health over a period of two months from august to September in the year 2014.

This Institute is the tertiary level referral centre for the urban and rural state population.

The study was approved by the Ethical Committee of Madras Medical College. A formal written consent in the mother tongue was obtained from all participants included in the study.

All participating patients were given the information sheet pertaining to the nature of study.

Sample of the study

The Study group was recruited from the newly attending op clinic and inpatient ward with first episode, and drug naive.

The first episode schizophrenia is defined as patients attending first time to a psychiatry service with a psychotic episode without past history of any mental disorders.

The study group consisted of sixty consecutive schizophrenic patients, who are classified in to positive and negative subtype by using positive and negative syndrome scale.

We considered patients who scored “moderate” or higher on at least three of the seven positive items as positive-type schizophrenics and those with the reverse Pattern (“moderate” on at least three negative items) as negative type schizophrenics considering the results from this scale, we divided participants into two groups: positive subtype (30 patients) and negative subtype (30 patients).

INCLUSION CRITERIA:

- 1) Patients fulfilling ICD 10 criteria for schizophrenia.
- 2) Age;20-60 years, sex; both male and female .
- 3) With minimum requirement of primary education.
- 4) Thirty patients with positive symptoms and thirty patients with negative symptoms.

EXCLUSION CRITERIA

- 1) Psychotic disorders secondary to general medical condition/Neurological disorders.
- 2) Psychotic disorders secondary to Alcohol/ Other substance disorders.

- 3) Psychotic disorders in the presence of subnormal intelligence.
- 4) psychotic states secondary to other mental disorders ie. Mood disorders with psychotic symptoms.

ASSESSMENT INSTRUMENTS

1) ICD I0 diagnostic criteria for diagnosing psychiatric disorders

2) Semi-Structured Pro forma, to collect Socio demo graphic data, Family History, Disease type, Onset of age,Duration of illness, and its details,.

3) Information on clinical symptom severity was obtained by using the Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1989).

4) Neurological Evaluation scale (Heinrich and Buchanan in 1988) with its requirements (cards for audio visual integration tests, objects for stereo gnosis).

5) Self structured NSS scoring sheets.

ICD-10 Diagnostic Criteria for Schizophrenia:

General criteria for Paranoid, Hebephrenic, Catatonic and Undifferentiated type of Schizophrenia:

G1.Either at least one of the syndromes, symptoms and signs listed below under (1), or at least two of the symptoms and signs listed under

(2), should be present for most of the time during an episode of psychotic illness lasting for at least one month (or at some time during most of the days).

1. At least one of the following:

    a. Thought echo, thought insertion or withdrawal, or thought broadcasting.

    b. Delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception.

    c. Hallucinatory voices giving a running commentary on the patient's behaviour, or discussing him between themselves, or other types of hallucinatory voices coming from some part of the body.

    d. Persistent delusions of other kinds that are culturally inappropriate and completely impossible (e.g., being able to control the weather, or being in communication with aliens from another world).

2. Or at least two of the following:

    a. Persistent hallucinations in any modality, when occurring every day for at least one month, when accompanied by

delusions (which may be fleeting or half-formed) without clear affective content, or when accompanied by persistent over-valued ideas.

b. Neologisms, breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech.

c. Catatonic behaviour, such as excitement, posturing or waxy flexibility, negativism, mutism and stupor.

d. "Negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses (it must be clear that these are not due to depression or to neuroleptic medication).

G2.Most commonly used exclusion criteria: If the patient also meets criteria for

- Manic episode or depressive episode, the criteria listed under G1.1 and G1.2 above must have been met before the disturbance of mood developed.

G3.The disorder is not attributable to organic brain disease, or to alcohol- or drug related

- Intoxication, dependence or withdrawal.

Positive and negative syndrome scale (PANSS)

- **Overview**
- The PANSS was originated as a more rigorously operationlized method for evaluating positive, negative, and other symptom dimensions in schizophrenia. Initially, it had been formulated as a special adaption of two psychiatric rating scales, the BPRS (OVERALL & GORHAM, 1962) and the PSYCHOPATHOLGY RATING SCALE (Singh & kay, 1975),
- Which culled items that optimally represent positive and negative features of schizophrenia. As it evolved, however, the need for greater psychometric sophistication to successfully standardize the technique, including more detailed guidelines for eliciting and evaluating psychiatric symptoms. Accordingly, the interview procedure and all rated items were modified and expanded to provide precise instructions for conduct of the PANSS interview, clear-cut definitions for each parameter to be rated, distinct criteria for seven levels of psychopathology.
- The PANSS categories positive and negative symptoms according to the original conceptualization of T J CROW (1980a, 1980b)

The selection of items was guided by five considerations, in the following order of importance:

- Items must be consistent with the, theoretical concept of positive and negative psychopathology as representing productive features superadded to the mental status vs. deficit features characterized by loss of functioning (cf. Andreasen and Olsen 1982).
- As per Carpenter, Heinrichs, and Alphs (1985), items should comprise symptoms that can be unambiguously classified as positive or negative and which, by most accounts, are regarded as primary rather than derivative (as, for example, impaired attention, disorientation, and preoccupation may be secondary to arousal disorder or hallucinations).
- To the extent possible, they should include symptoms consensually regarded as crucial to the definition of the positive syndrome (e.g., hallucinations, delusions, and disorganized thinking) and negative syndrome (e.g., blunted affect, emotional withdrawal, and apathetic social withdrawal
- To optimize the content validity, they should sample from diverse realms of functioning, such as the cognitive, affective, social, and communication and

- For practical and psychometric reasons, such as facilitating cross-comparisons and equalizing reliability potential, the numbers of items included in the positive a nd negative scales should be the same.

  In addition to the seven positive and seven negative items, 16 symptoms that cannot be linked decisively to either syndrome are included and comprise a general psychopathology scale .As described by GUY (1976), five factor scores are also obtained by summing statistically related items; these factors are anergia, thought disturbances, activation, paranoid-belligerence, and depression.The general psychopathology and factor scores as reference points, or control measures, for interpreting the positive and negative symptoms scores..

PANNS INTERVIEW PROCEDURE

The information is derived from the family members, hospital staff and from clinical interview. Information regarding social impairments, impulse control, Hostility, passive with drawl, active social avoidance are derived from family Members. All other information is accured through psychiatric interview for 30 – 45 minutes – which helps in directly observing affective, psychomotor, cognitive, perceptual, attentional, integrative and interactive functions the interview contains four phases

Phase 1 (non directive phase) in the first 5 – 10 minutes patients are encouraged to discuss their history, current life situation, circumstances regarding their hospitalization. The objective of this phase is to establish a rapport and allow the patient to express areas of concern the interviewer during this un challenging, non directive phase observes the patients thought process, content, communication, rapport, judgment and insight, affective and motor responses

Phase 2

During this semi structured phase the interviewer determines the presence of productive symptoms (hallucinations, delusional ideation, suspiciousness and impaired insight) and the severity of these symptoms (prominence, frequency and interference in daily activities)

Phase 3

Structured phase – focusing on specific information regarding the patients mood state, anxiety, abstract reasoning ability and orientation to three spheres

Final phase concentrates on forceful questioning on areas where the patients seems to be defensive and uncooperative (ambivalent) in this phase the patient is subjected to greater stress and testing their limits

PANSS SCORING INSTRUCTIONS

The PANSS is scored by summation of ratings across items, such that the potential ranges are 7-49 for the Positive and Negative Scales and 16-112 for the General Psychopathology Scale. The Composite Scale is arrived at by subtracting the negative from positive score, thus yielding a bipolar index that ranges from -42 to +42. Which is essentially a differences score that reflects the degree of predominance of one syndrome in relation to the other and may serve for purposes of classification. Finally, one may add together all 30 items to provide a total psychopathology score re flects o n the severity of illness .

The PANSS may be used for typological assessment .It has been applied also as a method of characterizing schizophrenic patients with a predominantly positive vs. a predominantly negative syndrome. We considered patients who scored “moderate” or higher on at least three of the seven positive items as positive-type schizophrenics and those with the reverse pattern (“moderate” on at least three negative items) as negativetype schizophrenics**;** (LINDENMAYER, KAY, &OPLER, 1984) patients who qualified for both groups or neither were labeled as mixed type.

The Positive and Negative Syndrome Scale

The Positive and Negative Syndrome Scale is a measure of positive and negative schizophrenic symptoms and related aspects, such as cognitive, affective, and social functioning

. The test has 30 items:

- (a)7 items of which represent the positive symptoms;
- (b) 7 items are related to the negative symptoms; and
- © the remaining 16 items cover related aspects of general
- psychopathology and functioning.

Each item is rated on an interval scale ranging from 1 (absent) to 7 (extreme psychopathology).

The total scores may thus range between 30 and 210, with a higher score indicative of a more severe illness.

Neurological Evaluation Scale (NES)

The Neurological Evaluation Scale is a structured scale that presents scores in four subscales- sensory integration, motor coordination, sequencing of complex motor acts and others. Apart the tests for cerebral dominance it has 26 discrete items, of which 14 are tested bilaterally. Each ITEM IS SCORED USING anchored ratings of 0-normal, 1-mild, but definite impairement, 2-marked impairement except ffor the snout

and suck reflexs which are scored as either 0 or 2. The motor coordination subscale includes tandem walk, rapid alternating movements, finger thumb opposition, and the finger-nose test. The sensory integration subscale includes audio visual integration, stereognosis, graphesthesia, extincton, right/ lt confusion. sequencing of complex motor acts subscale includes the fist-ring test, fist-edge palm test, the ozeretski test and rhythm tapping test B.Others sub scale includes adventitious over flow, the Romberg test, tremor, memory, mirror movements, rhythm tapping test A, synkinesis, convergence, gsze impersistence, glabeelar reflex, snout reflex grasp reflex and suck reflex, . Higher scorres indicate neurological impairment in schizophrenia.

In this study the score of 2 was taken as positive for NSS.

NSS Scoring sheet 1 & 2

It contains individual items and its scorings as per NES, The scores of of individuals are marked during assessment.

NSS ASSESSMENT:

NSS assessment was done by the original version of neurological evaluation scale made in the op department. Cards were produced with rhythms for rhythm tapping and audio-visual integration test. For the stereognosis test participants were asked to identify pencap, coins, eraser,

and a sellotap coil. Two items were identified in each hand. The administration of the NES took approximately 45 minutes to complete.

Data collection:

The scores of individuals items were marked in NSS scoring sheet-1 during assessment. Then the positive scores(score 2) of individuals alone were entered in NSS Scoring sheet II. The positivity of individuals for entered in Master chart and data analysed.

Statistical Analysis:

The study subjects of Positive and Negative subtype of schizophrenia were described and matched according to their socio economic and demographic profiles in terms of descriptive statistics and interpreted for matching by inferential statistics. The continuous variables were interpreted by students t test and categorical variables were interpreted by χ^2 (Chi-square) test. The interactions of Soft Neurological Signs (NSS) with Positive and Negative subtype of schizophrenia were analyzed and interpreted by Binary Logistic Regression. The above statistical procedures have been performed with the help of the statistical package namely IBM SPSS Statistics-20. The P-values <0.05 were treated as significant in two tailed test.

RESULTS

Description and matching of the study subjects:

The study subjects of positive and negative schizophrenia were described and matched for comparison of NSS. The socio economic and demographic profiles described and matched were age, sex, education, occupation, marital status, Socio economic status, family history, duration of illness and handedness.

Table-1:

Description of subjects according to their age:

age: group	Negative		Positive		Total	
	No	%	No	%	No	%
20-24	5	16.7	9	30.0	14	23.3
25-29	9	30.0	3	10.0	12	20.0
30-34	7	23.3	7	23.3	14	23.3
35-39	5	16.7	7	23.3	12	20.0
40-44	4	13.3	4	13.4	8	13.4
Total	30	100.0	30	100.0	60	100.0
Range	20-44		20-44		20-44	

The table-1 states the percentage distribution of the negative and positive groups with a range of 20-44years.

Graph 1 :

Description of subjects according to their age

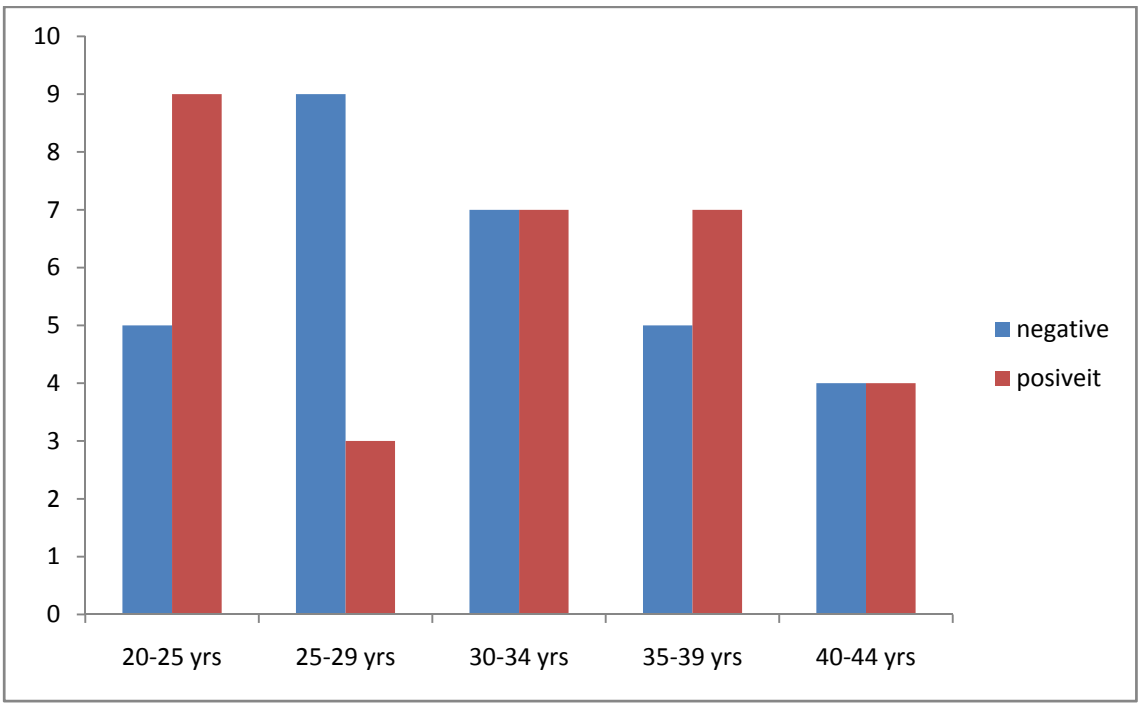


Table-2:

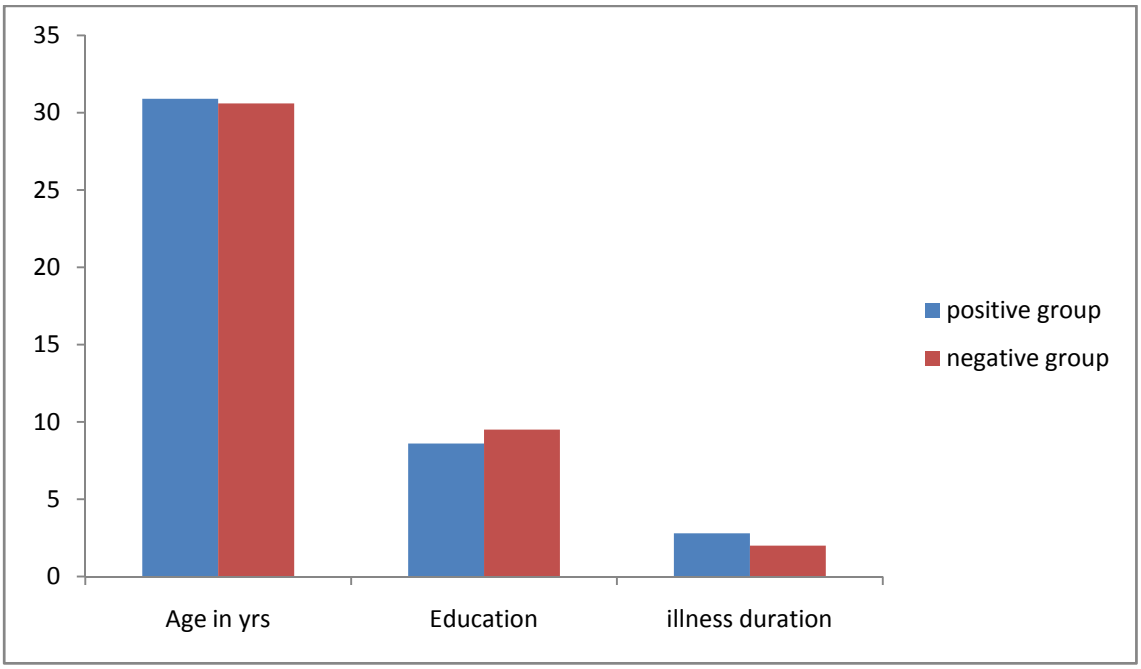
Matching of subjects according to their age, education and illness:

	Negative		Positive		Difference b/w. means	t	d f	Significance
	Mean	**SD**	**Mean**	**SD**				
Age	30.9	6.8	30.6	7.0	0.3	0.130	58	P=0.897
Education	8.6	2.9	9.5	3.6	0.9	1.025	58	P=0.070
Illness	2.8	1.7	2.0	1.7	0.8	1.888	58	P=0.064

The table-2 matches the negative and positive groups in respect of the age, education and duration of illness.

Graph 2 :

Matching of subjects according to their age, education and illness



The mean ages of both groups were 30.9±6.8 and 30.6±7.0 years. The difference of ages between the two groups was not statistically significant (P>0.05). The mean educations in years of both groups were 8.6±2.9 and 9.5±3.6 years. The difference of education between the two groups was not statistically significant (P>0.05). The mean durations of illness of both groups were 2.8±1.7 and 2.0±1.7 years. The difference of ages between the two groups was not statistically significant (P>0.05).

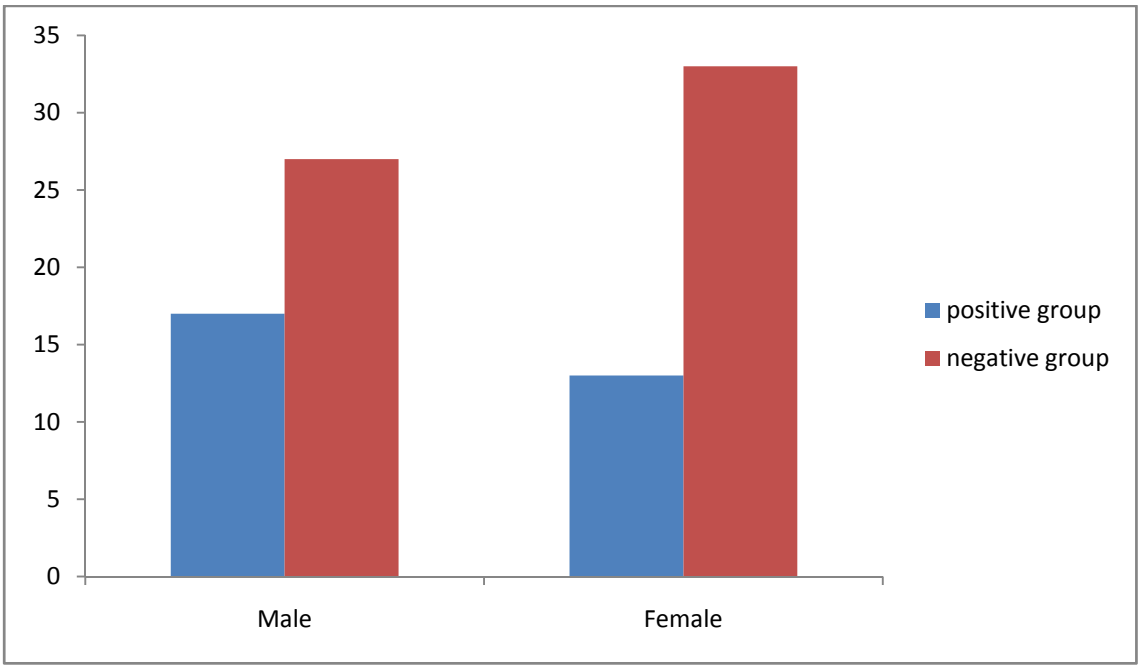
Table-3:

Gender wise matching of Negative and Positive groups:

Gender	**Number of persons**			χ^2	**df**	**Significance**
	Negative	**Positive**	**Total**			
Male	17	10	27	3.300	1	P=0.069
Female	13	20	33			
Total	30	30	60			

Graph : 3

Gender wise matching of Negative and Positive groups



The table-3 matches the gender between the two groups. The results revealed that the gender did not have any statistically significant difference between the negative and positive schizophrenia subjects (P>0.05).

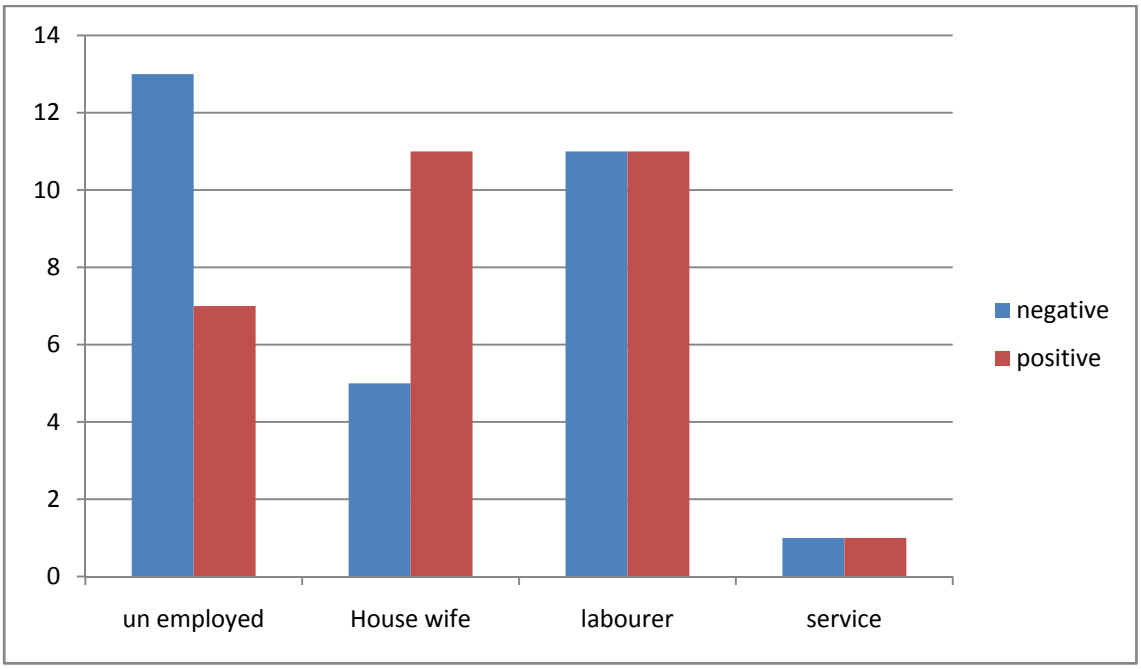
Table-4:

Matching of Negative and Positive subjects according to occupation:

Occupation	Number of persons			χ^2	df	Significance
	Negative	Positive	Total			
Un employed	13	7	20	4.050	2	P=0.256
House Wife	5	11	16			
Labourer	11	11	22			
Service	1	1	2			
Total	30	30	60			

Graph : 4

Matching of Negative and Positive subjects according to occupation



The results revealed that the occupation did not have any statistically significant difference between the negative and positive schizophrenia subjects (P>0.05).

Table-5:

Matching of Negative and Positive subjects

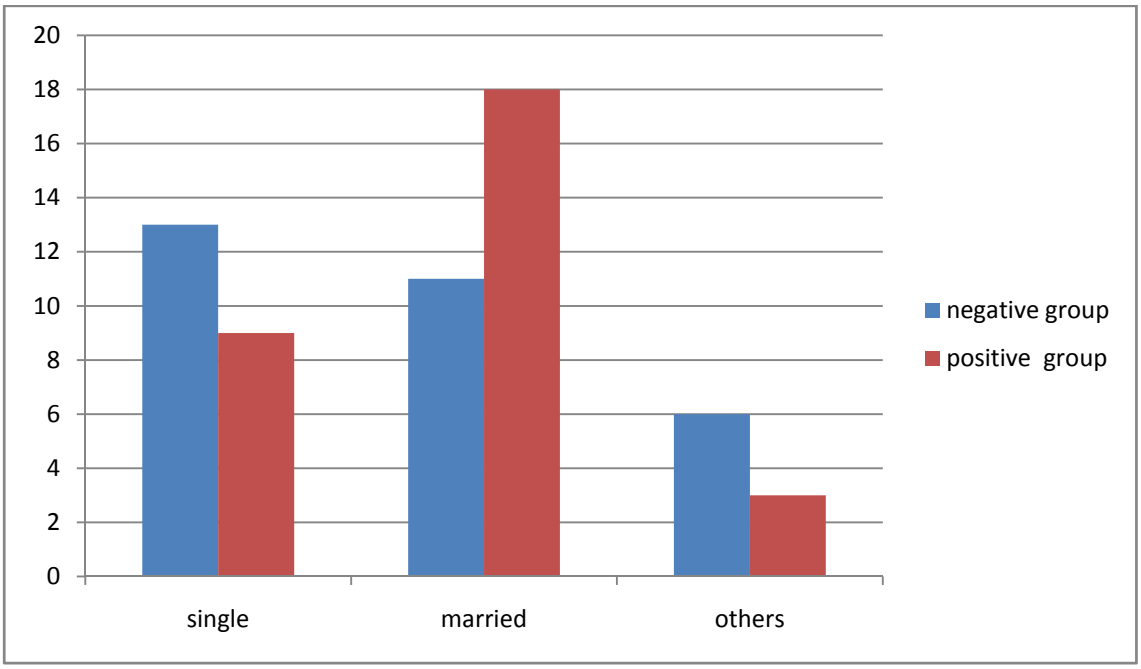
according to marital status:

Marital status	Number of persons			χ^2	df	Significance
	Negative	Positive	Total			
Single	13	9	22	3. 417	2	P=0.181
Married	11	18	29			
others	6	3	9			
Total	30	30	60			

Graph-5:

Matching of Negative and Positive subjects

according to marital status:



The table-5 matches the marital status between the two groups. The results revealed that the marital status did not have any statistically significant difference between the negative and positive schizophrenia subjects (P>0.05).

Table-6:

Matching of Negative and Positive subjects

according to Socio economic status:

Socio economic status	Number of persons			χ^2	df	Significance
	Negative	Positive	Total			
Low	25	27	52	0.577	1	P=0.448
Middle	5	3	8			
Total	30	30	60			

The table-6 states the matching of the socio economic status between the two groups. The results revealed that the socio economic status did not have any statistically significant difference between the negative and positive schizophrenia subjects (P>0.05).

Table-7:

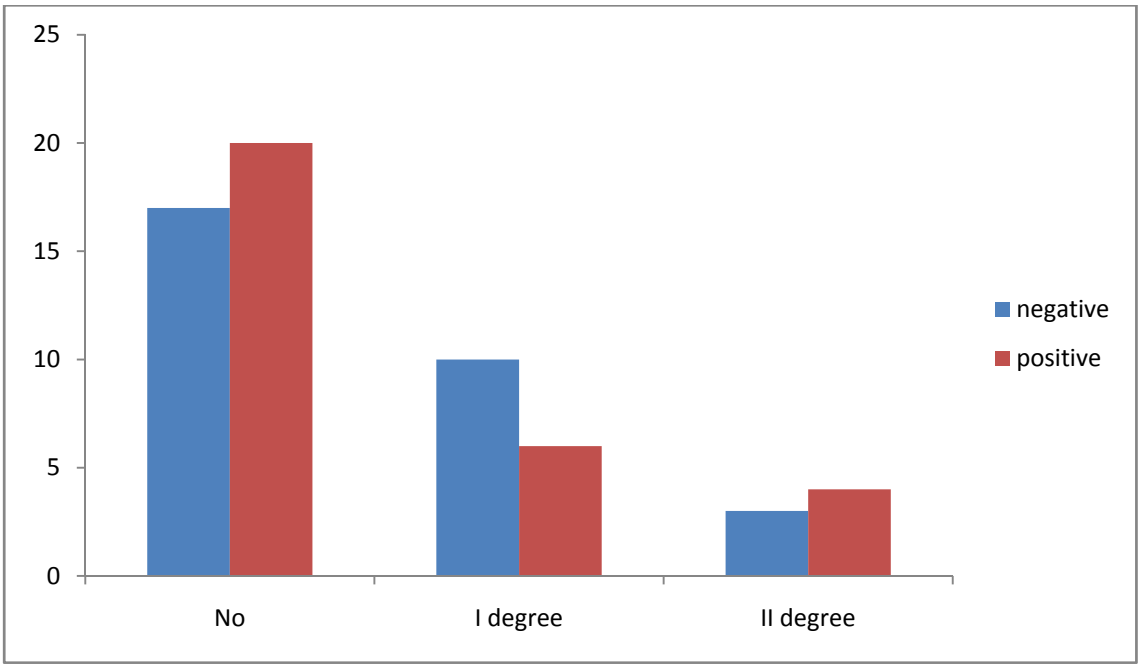
Matching of Negative and Positive subjects

according to family history:

Family history	Number of persons			χ^2	df	Signi-ficance
	Negative	Positive	Total			
No	17	20	37	1. 386	2	P=0.181
1st degree	10	6	16			
2nd degree	3	4	7			
Total	30	30	60			

Graph-6:

Matching of Negative and Positive subjects according to family history



The table-7 states the matching of the family history between the two groups. The results revealed that the family history did not have any statistically significant difference between the negative and positive schizophrenia subjects (P>0.05).

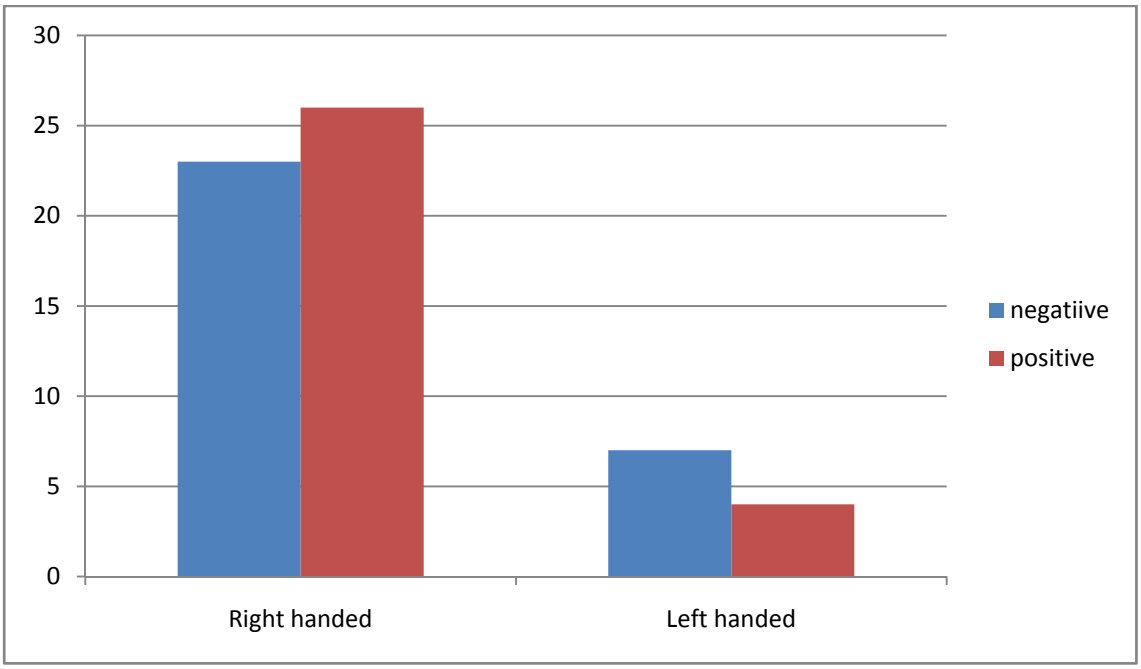
Table-8:

Matching of Negative and Positive subjects according to handedness:

handedness	Number of persons			χ^2	df	Significance
	Negative	Positive	Total			
Right hand	23	26		1. .002	1	P=0.317
Mixed	7	4				
Total	30	30	60			

Graph 7:

Matching of Negative and Positive subjects according to handedness



The table-8, the results revealed that the handedness did not have any statistically significant difference between the negative and positive schizophrenia subjects (P>0.05).

The above analysis and interpretations evidenced that the two groups were not statistically significantly differed in respect of their age, sex, education, occupation, marital status, Socio economic status, family history, duration of illness and handedness. Hence the groups are comparable groups.

Mean of Positive and Negative PANSS Score

Table-9:

Mean of Positive and Negative PANSS Score:

Scores	Mean	Standard Deviation
Positive	32.0	5.5
Negative	31.4	7.1

The table 9 Shows the mean scores in the positive symptom subscale of Panss and negative symptom subscale of panss. The negative symptoms mean score was found to be 31.4±7.1. and the positive symptoms mean score was 32.0±5.5

Comparison of NSS between positive and negative sub type

Table-10:

The percentage distribution of subjects with positive score (2score)

Sensory integration against individual item of NES:

Sl. No	Sensory integration	Negative n=30		Positive n=30	
		Frequency	%	Frequency	%
1	Av integration	22	73.3	24	76.7
2	Stereognosis Rt	2	6.7	0	0.0
3	Stereognosis Lt	1	3.3	0	0.0
4	Graph aesthesia Rt	17	56.7	17	56.7
5	Graph aesthesia Lt	22	73.3	15	50.0
6	Extinction	1	3.3	0	0.0
7	R and L confusion	10	33.3	0	0.0

Table-11:

The percentage distribution of subjects with positive score (2score)

Motor Coordination against individual item of NES:

Sl. No	Motor Coordination	Negative n=30		Positive n=30	
		Frequency	%	Frequency	%
1	Tandem walk	10	33.3	1	3.3
2	Rapid alternative movements Rt.	6	20.0	5	16.7
3	Rapid alternative movements Lt.	6	20.0	5	16.7
4	Finger thumb opposition Rt.	7	23.3	0	0.0
5	Finger thumb opposition Lt.	7	23.3	0	0.0
6	Finger nose test Rt.	1	3.3	0	0.0
7	Finger nose test Lt.	1	3.3	2	6.7

Table-12:

The percentage distribution of subjects with positive score (2score)

Sequences of complex motor acts against individual item of NES:

Sl. No	Sequences of complex motor acts	Negative n=30		Positive n=30	
		Frequency	%	Frequency	%
1	Fist ring test Rt.	11	36.7	12	40.0
2	Fist ring test Lt.	13	43.3	12	40.0
3	Fist edge palm Rt.	16	53.3	12	40.0
4	Fist edge palm Lt.	18	60.0	11	36.7
5	Ozeretski test	10	33.3	11	36.7
6	Rhythm tapping B	26	86.7	25	83.3

Table-13:

The percentage distribution of subjects with positive score (2score)

Others against individual item of NES:

Sl. No	Others	Negative n=30		Positive n=30	
		Frequency	%	Frequency	%
1	Synkinesis Right	17	56.7	4	13.3
2	Synkinesis Left	17	56.7	4	13.3
3	Converge Right	17	56.7	3	10.0
4	Converge Left	19	63.3	3	10.0
5	Gaze Right	15	50.0	12	40.0
6	Gaze Left	15	50.0	11	36.7
7	Glabbellar tap	20	66.7	5	16.7
8	Grasp Right	3	10.0	1	3.3
9	Grasp Left	3	10.0	0	0.0
10	Snout reflex	3	10.0	3	10.0
11	Suck reflex	2	6.7	0	0.0
12	Mirror movement Right	4	13.3	0	0.0
13	Mirror movement Left	4	13.3	0	0.0
14	Romberg sign	5	16.7	0	0.0
15	Adventitious overflow Right	4	13.3	0	0.0
16	Adventitious overflow Left	4	13.3	0	0.0
17	Tremor Right	8	26.7	0	0.0
18	Tremor Left	8	26.7	2	6.7
19	Production	22	73.3	14	46.7
20	Memory 10 minutes	16	53.3	16	53.3
21	Memory 5 minutes	12	40.0	14	46.7

Comparison of NSS between positive and negative sub type:

Table-14:

Comparison of NSS between positive and negative groups:

NSS	Positive		Negative		Differ b/w. Means	t	d f	Significance
	Mean	SD	Mean	SD				
Sensory Integration	5.0	1.7	6.7	2.6	1.7	2.931	58	P=0.005
Motor Coordination	3.2	1.8	4.6	3.8	1.4	1.730	58	P=0.089
Seq. of Com. Mot Act	6.9	3.9	7.8	3.2	0.9	0.978	58	P=0.332
Others	14.0	6.1	19.0	7.8	5.0	2.793	58	P=0.007
Total	29.1	10.2	38.1	15.4	9.0	2.783	58	P=0.007

The table-14 states the comparison between positive and negative subtype schizophrenia subjects' NSS scores. The mean sensory integration scores of positive and negative subtype subjects were 5.0±1.7 and 6.7±2.6 respectively. The difference was statistically highly significant (P<0.01). The mean motor coordination scores of positive and negative subtype subjects were 3.2±1.8 and 4.6±3.8 respectively. The difference was not statistically significant (P>0.05). The mean sequencing of complex motor acts scores of positive and negative subtype subjects were 6.9±3.9 and 7.8±6.1 respectively. The difference was not statistically significant (P>0.05). The mean other NSS scores of positive

and negative subtype subjects were 14.0±6.1 and 19.0±7.8 respectively. The difference was statistically highly significant (P<0.01). The mean total NSS scores of positive and negative subtype subjects were 29.1±10.2 and 38.1±15.4 respectively. The difference was statistically highly significant (P<0.01).

Comparison of interaction between NSS with positive and negative groups:

The interactions of NSS scores with the positive and negative sub type schizophrenia subjects were studied by binary logistic regression analysis. The enter method was adopted and results were furnished below.

Table-15:

Interactions between NSS scores Category with positive and negative sub type schizophrenia subjects:

Blocks	NSS scores Category	Wald - χ^2	df	Significance
1	Sensory Integration	6.478	1	P=0.011
2	Sensory Integration	4.304	1	P=0.039
	Motor Coordination	0.014	1	P=0.906
3	Sensory Integration	4.349	1	P=0. 037
	Motor Coordination	0.003	1	P=0.957
	Sequencing of Complex Motor Acts	0.018	1	P=0.893
4	Sensory Integration	2.798	1	P=0.094
	Motor Coordination	0.220	1	P=0.639
	Sequencing of Complex Motor Acts	0.855	1	P=0.355
	Others	3.017	1	P=0.082

The Table-15 shows the interactions between NSS scores Category with positive and negative sub type schizophrenia subjects. The block wise enter method results revealed as below.

- Block 1. Sensory integration was statistically significantly differed between the positive and negative groups (P<0.).
- Block-2. Sensory integration was significant (P<0.05) and Motor Coordination was not significant (P>0.05).

- Block-3. Sensory Integration was statistically significant (P<0.05). Motor Coordination and Sequencing of Complex Motor Acts were not statistically significantly differed (P>0.05).

- At Block-4. All four NSS score categories had not been statistically significantly differed with positive and negative sub type schizophrenia subjects (P>0.05).

The non significant results were attributed to the interactions effect between the NSS scores category.

DISCUSSION

This study was conducted in the outpatient and inpatient ward in the Institute of Mental Health, Madras Medical College Hospital. Ethical Committee approval for conducting the study was obtained from the Institutional Ethical committee in august 2014 (annexure).

The study was carried out in the period between august and September 2014.

The study groups are selected based on the ICD 10 diagnostic criteria and PANSS Scoring. The sample was selected by stratified random sampling. An information sheet (annexure) regarding the illness, and the purpose of the study was provided to the patient.

Informed consent was obtained in the mother tongue. And then written consent was obtained (annexure).Only those patients who consented to participate in the study and were cooperative for interview were recruited.

DEMOGRAPHIC AND CLINICAL DATA

The two samples do not significantly differ in terms of age, gender, marital status, religion, educational status, occupation, and domicile distribution. The study population consists of a majority of individuals in the age group of 25 – 44 years among both groups. Both males and

females are almost equally represented among both groups. There are a greater number of single subjects as compared to married individuals in both the groups studied and a majority of the subjects in this study are Hindus.

The study group had 33 females and 27 males of which patients with positive symptoms of schizophrenia were 20 females and 10 males. These Patients had a mean age of 30.6±7.0 years and mean years of education was 9.5±3.6 years, The mean duration of illness was 2.0±1.7 years.

Among patients with negative symptoms of schizophrenia, there were 17 males 13 females. This group had a mean age of 30.9±6.8years, and a mean age of educations was 8.6±2.9, mean duration of illness was 2.8±1.7 years.

The study groups were matched in respect of their sex, age, education, duration of illness, occupation, social status, family history, type of family and marital status in positive and negative symptom subgroup.

Comparison with sexual differences in schizophrenia and NSS:

Our results showed that there are no sex differences in the presence and severity of positive and negative study groups. (Table 3)

In contrast to this, Males with schizophrenia have a far worse outcome than females .According to Lewine and Goldstein, males are more frequently exhibit classic and negative symptoms of schizophrenia. Male schizophrenic patients are found to have more cognitive (Haas et al. 1990) and neurologic abnormalities (Marcus et al.1985).

Most of the studies showed no variance in the presence and severity of NSS except one study showed female patients with a family history of schizophrenia had high NSS score (Abbie Lane et al 1996) . Duggal et al illustrated that performance in motor sequencing tasks may be influenced by sex-bound variables.

Comparison of Age in schizophrenia:

In our study, regarding age and education there are no significant differences in both the groups(table 2).

Age at onset data from the Indian population studies have shown significantly higher Proportion of females as compared to males who had age at onset younger than 20 years. Analysis of the data of all patients with age at onset of 30 years or younger also confirmed that there were significant sex differences. This contrasts with the data from other global studies elsewhere suggesting that younger age at onset in males is not a universal phenomenon.

Few studies have found positive correlation between older age and more NSS and an inverse correlation between education and neurological impairment in patients with first episode schizophrenia. (Cuesta, Mohr et al)

One recent study found earlier onset of illness in the negative subtype patients, therefore indicating a deeper neurological impairment .

Comparison with Duration of illness in schizophrenia:

In our studies shows no positive correlation in duration of illness in both study groups. This findings are similar to the study by **Venkatasubramanian.G etal 2OO3.**

OTHER SOCIODEMOGRAPHICDATA IN SCHIZOPHRENIA:

There is no significance in occupation, maritalstatus socioeconomic status, family history.

Similarly one study reported an inverse correlation between social class and soft and hard neurological signs**.**

Handedness and schizophrenia:

There is no significant different between both positive and negative symptoms.

Comparison of positive and negative score in PANSS:

In table 9 thus we see that the mean of positive symptoms was greater than the negative symptoms in our study.

RELATIONSHIP OF SOFT NEUROLOGICAL SIGNS WITH POSITIVE ANDNEGATIVE SYNDROME OF SCHIZOPHRENIA:

The neurological soft signs in this study were evaluated using the Neurological Evaluation Scale and the mean NES score among positive type patients was found to be 29.1±10.2 and for negative 38.1±15.4 This scale has been used in most of the published studies in this area. In an earlier study by Venkatasubramanian et al (2001), the mean NES total score was 17.1 with a standard deviation of 6.973. A study by Varambally et al showed a mean NES score of 21.38 with a standard deviation of 9.23 among schizophrenia patients. The comparison of the mean NES scores among positive and negative subtype in our study reveals that both are highly significant and there is no difference between the two groups studied. This suggests that neurological soft signs are highly prevalent among patients with schizophrenia.

In these studies the total NES score alone was studied. In our study we compare the NES scores among the positive and negative subscales of PANSS. There are no earlier Indian studies with such comparison.

The results individual items are shown in Tables 10, 11, 12, 13. These table shows the number and percentage of the subjects with positive score (score 2) against individual items of NE.S

In Table 10 -we have compared individual item of sensory integrated sign in both positive and negative subtype.

- In Negative group, Stereo gnosis (both left and Right),Right and Left confusion, Extinction were more prevalent compared to the positive group.
- In positive group there is no involvement of, Stereo gnosis (both left and Right), Right and Left confusion, Extinction.
- Graph aesthesia is more prevalent in negative group where as equal in both positive and negative group.
- Audiovisual integration affected in both group but subtly high in positive group76.7% where as previous studies AV integration was affected more in negative group, in our study it was slightly more prevalent in the positive group(76.7% among negative group)
- Overall our results shows sensory integration is mainly involved in negative group .
- In a study by Bombin Arango 2005, the correlation coefficients between NSS total and total, positive and

negative symptoms scores indicate shared variance from 2% to 10%, with the weakest relation between NSS and positive symptom severity.

Comparison of motor coordination in schizophrenic sub type:

In table 11, motor coordination signs are individualy analysed both left and right between positve, and negative group

- Tandem walking was more affected in the negative group (33.3%) as compared to the positive group(3.3%).
- Left finger nose test is more affected in positive group (6.7%)
- Right finger thumb opposition and left finger thumb opposition and finger nose test(right) were nott affected in the positive group.
- Tandem walking;this correlates with previous studies which state tandem walking difficulty is prevalent I negative symptom group.
- In our study population, total symptom scale of motor in coordination is more prevalent among negative group which is different from past studies which have stated the vice versa.

Comparision of Sequences of complex motor acts in Positive and negative subtype of schizophrenia:

- The individual items analyzed in table 12,
- the results shows all the signs equally affected in both sides in both negative and positive group except Fist edge palm Lt 60% in negative group compared to positive 36.7%.
- And Fist edgepalm test (right) 53.3% in negative group compared to positive (40%)
- Several number of studies reported that Sequences of complex motor acts are commonly involved in negative group (Tiryaki et al, Tijana Cvetic et al) but our results shows similar prevalence in 4 items.

Comparison of Others items in Positive and negative subtype of schizophrenia:

In Table 13 Others individual items are analyzed.

- In negative group more than 50%(15/30) patients affected in Synkinesis, Convergence, gaze impersistence, glabellar tap also rhythm reproduction are associated in negative group compared to positive group.

- Regarding frontal release signs which is only involved in negative group. This is similar to one study by prikryl R,Ceskova et al who state that negative symptoms score highly correlated with 'others' NES sub score.
- In our study 10 minites memory score was equal in both positive and negative where as 5mts score was lower in negative subtype.
- This is similar to one other study Verbal memory in schizophrenia found that negative symptoms were the only significant variable affecting performance (Aleman et al.)

Total NES score compared in positive and subtype:

In this study NES mean score compared with PANSS positive and negative type by using 'student t' test .

- In negative subtype there is high mean score in sensory integration and others items which is statistically significant p value $p<0.01$,and mean total NES score also high.
- Several other studies have demonstrated the positive relationship of softneurological signs with negative symptoms (Schroeder et al79, Wong et al80).

Comparison of NSS interaction: In this study, sensory integration compared to motor, sequencing complex motor and other items .Results (table15)shows it is highly significant in negative and final results are there is no significant differences($p>0.05$). in all signs in both groups. . To summarise,

Previous studies have examined specifically the relationship between the positive and negative syndrome in patients of schizophrenia and the presence of soft neurological signs. Neurological abnormalities have been correlated with the total number of psychiatric symptoms by Tucker and Silberfarb75. Several other studies have demonstrated the positive relationship of soft neurological signs with negative symptoms (Schroeder et al79, Wong et al80).

Also several studies refuting any relationship of soft neurological signs with both positive and negative symptoms (Kolakowskaet al, Barkto et al,Chen et al, Malla et al).

The results of our study appear to be consistent with previous studies which have demonstrated a significant relationship of few soft neurological signs with both positive negative symptoms in schizophreniaand no significant relation of few other NSS.

SUMMARY

This is a observational clinical cross sectional descriptive study assessing and comparing soft neurological signs, in positive and negative schizophrenia patients.

Both types of patients are matched in terms of age, gender, marital status, religion, educational status, occupation and domicile.

This study shows the presence of soft neurological signs in schizophrenia patients. This study does not show any correlation between age, gender, educational status and duration of illness with the presence of soft neurological signs in Schizophrenia patients.

Statistically there is no significant positive correlations are observed between the negative and positive symptom subscale of PANSS and the NES scores among the patients with schizophrenia.

Among the NES Subscales, sensory integration and others items in NES score are Statistically significant positive in negative type of schizophrenic patients.

CONCLUSION

Patients with schizophrenia exhibit more neurological signs than normal comparison subjects; That NSS are significantly increased in schizophrenia is in line with the results of a wealth of previously existing studies of schizophrenia and related psychotic disorders. NSS did not seem to be aggravated by neuroleptic drug treatment, supporting the respective results of previous studies. NSS are associated with psychopathological symptoms; hence, the highest scores were found in the acute psychotic state. In follow-up studies, NSS typically decreased with remission of acute symptoms. While this effect is more pronounced in patients with a favorable rather than a more chronic course of the disease, even the NSS scores of the former remain significantly higher than in healthy control groups. These effects do not correspond to potential confounders, specifically neuroleptic side effects, age, or gender.

Although the use of comprehensive structured scales assessing neurological abnormalities is still more appropriate to the research setting, a regular physical examination incorporating the neurological system and the evaluation of hard signs and soft signs, as well as signs of extrapyramidal symptoms, should figure in the assessment and treatment of any patient with psychosis and schizophrenia. This examination should be conducted early in the course of the illness, ideally before treatment is

initiated, and at regular intervals thereafter. To achieve this, psychiatrists should work to develop and maintain the skills necessary to identify these neurological clinical signs reliably, and view their periodic assessment as much a part of the patient assessment as the mental state examination. It has been proposed that cortical release signs (e.g. palmomental, grasp and oral reflexes) should be routinely evaluated in addition to the standard neurological examination, as these signs may be indicators of diffuse cerebral dysfunction requiring further investigation. In addition, audio-visual integration and verbal memory offer both high specificity and predictive value in schizophrenia, which may help to inform diagnosis at first presentation and inform predictions of future treatment response. In this presenting study also similar to above findings and there is significant evidence to suggest that NSS including cerebellar signs may form an intrinsic part of the syndrome of schizophrenia. This lends strength to the neurodevelopmental hypothesis for the etiopathogenesis of schizophrenia as well as the model of "cognitive dysmetria" to explain some of the features seen in this enigmatic disorder. Also, examination for cerebellar abnormalities in schizophrenia patients might help in objectively identifying those with potentially poorer prognosis. A focused, regular neurological evaluation can then provide important prognostic information regarding the risk of negative symptoms and cognitive deficits and can help to identify individuals with more complex future care needs.

LIMITATIONS AND MERITS:

The present study is carried out in Institute of mental health, MMC, Chennai in a limited period of time during August- September 2014.

The population of this study is a selected one which does not have the characteristics of the general population of patients with schizophrenia. Hence the samples are not representative of the general population.

Recruitment of consecutive patients ensures that there is no sample bias. The exclusion and inclusion criteria are specific. Hence the sample consists of schizophrenia patients who are not suffering from any other psychiatric or medical illnesses, but this has not been verified by using specific investigations to exclude presence of such factors. The effect of anti-psychotics and other medications has not been considered in this study. The sample consists of only schizophrenia and excludes other types of psychotic disorders, which are also known to be associated with neurological impairment. The size of the sample and control is sufficient to calculate the prevalence of soft neurological signs in schizophrenia, but a larger sample size will be required to enhance the reliability and validity of the results. A larger sample size is required to calculate the exact relationship of soft neurological signs in schizophrenia patients and socio-demographic and clinical variables. The present study is a cross

sectional descriptive study examining the presence of soft neurological signs in positive and negative schizophrenia patients. The subjects are assessed on one occasion only. The tools used have adequate established reliability and validity. All the tools are rater friendly, easy to administer, less time consuming thereby causing no discomfort to the patients. The assessment is not blind due to study constraints, therefore rater bias is possible. Absence of sample selection bias, homogenous uncompromised sample of schizophrenia patients and detailed assessment of sub- groups of neurological soft signs also compared with subtypes of schizophrenia are notable merits of this study.

Despite its limitations the present study definitely indicates that there is a significant relationship between neurological soft signs andschizophrenia. This is the unique finding of this study. Further research is required, to establish this fact with adequate reliability and validity.

Future research should ideally address the following issues:

- Selection of representative population and sample.
- Larger sample size.
- Control groups of different types of psychotic disorders should be included.

- Comparative study of neurological impairments in schizophrenia patient with or without medication history.
- Use of more appropriate tools for assessment.
- Blind assessment.
- Prospective assessment on multiple occasions.

FUTURE DIRECTIONS

- Standardized objective measurement of NSS needs to be implemented to increase the objectivity of the assessment.
- Clinically, agreement on cut-off scores which may indicate possible poorer prognosis can lead to early initiation of effective treatments in these patients.
- Ongoing advances in imaging techniques and kinesiology may help further clarify the underlying neural substrates between NSS and neurocognitive functioning.
- Combining standardized measurement of NSS with MPAs and other areas of dysfunction in schizophrenia like Facial Emotion Recognition Deficits (FERD) may help in improving specificity and also in the development of a viable endophenotype.

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PROFORMA

1.	Name:	
2.	Hospital No:	
3.	Age:	1) 18-25 yrs 2) 25-35 yrs 3) 35-40 yrs 4) 40-60yrs
4.	Sex	1) Male 2) Female
5.	Address:	
6.	Occupation:	1) House Wife 2) Service class 3) Business class 4) Labour class 5) Students 6) Unemployed
7.	Marital Status:	1) Married 2) Divorced 3) Separated 4) Unmarried
8.	Education:	1) Uneducated 2) High School 3) Higher Secondary 4) Graduate 5) Post Graduate
9.	Religion:	1) Hinduism 2) Christianity 3) Islam 4) Others
10.	Socioeconomic Status:	1)Upper 2)UpperMiddle 3)Lower middle 4)Upper lower 5)Lower
11.	Locality:	1) Urban 2) Rural
12.	Informants	
13.	Complaints&duration	

14.	Past history	
15.	Age of Onset of illness:	1) <15 yrs 2) 16 – 20 yrs 3) 21 – 30 yrs 4) 31 -40 yrs 5) 40-60yrs
16.	Substance abuse:	1) Alcoholism 2) Nicotine 3) Polysubstance Nil
17.	Family History of Mental illness:	1) Yes 2) No
18	Personal History	1) 2) 3)
19.	Patient Compliance:	1) Good 2) Fair 3) Poor
20.	General physical examination	1) Pulse; 2) BP: 3) Fundus: RE LE 4) CVS: 5) RS: Abdomen
21	Mental status Examination	
22.	Diagnosis	
23.	PANSS	
24.	Neurological signs assessment	

NEUROLOGICAL SIGNS SCORING SHEET-II

	Case/ Control No.:							
ITEMS:								
SENSORY INTEGRATION								
	Audio Visual Intergation							
	Steriognosis							
		Right						
		Left						
	Graphesthesia							
		Right						
		Left						
	Extinction							
	R/L Confusion							
MOTOR CO- ORDINATION								
	Tandem walk							
	Rapid alternating Movements							
		Right						
		Left						
	Finger thumb opposition							
		Right						
		Left						
	Finger - Nose test							
		Right						
		Left						
SEQUENCING OF COMPLEX								
MOTOR ACTS								
	Fist - ring							
		Right						
		Left						
	Fist- edge - palm							
		Right						
		Left						
	Ozeretski							
	Rhythm tapping B							
OTHERS								
	Adventitious overflow							
		Right						

Left							
Romberg							
Treumor							
Right							
Left							
Memory							
5 min							
10 min							
Rhythm tapping A							
mirror movements							
Right							
Left							
Synkinesis							
Right							
Left							
Convergence							
Right							
Left							
Gaze Impersistence							
Right							
Left							
Glabellar reflex							
Snout reflex							
Grasp reflex							
Right							
Left							
Suck reflex							

		NEUROLOGICAL SIGNS SCORING SHEET I					
		Patient/Control Name :					
	Handedness				R	L	M
	Footedness				R	L	M
	Eyedness				R	L	M
	Cerebral dominence :				R	L	
1	Memory						
	5 min				0	1	2
	10 min				0	1	2
2	Stereognosis						
	Right				0	1	2
	Left				0	1	2
3	Graphasthesia						
	Right				0	1	2
	Left				0	1	2
4	Extinction				0	1	2
5	Right &Left confusion				0	1	2
6	Synkinesis						
	Right				0	1	2
	Left				0	1	2
7	Convergence						
	Right				0	1	2
	Left				0	1	2
8	Gaze Impersistence						
	Right				0	1	2
	Left				0	1	2
9	Glabellar tap reflex				0	1	2
10	Grasp reflx						
	Right				0	1	2
	Left				0	1	2
11	Snout Reflex				0		2
12	Suck reflex				0		2
13	Rapid alternating Movements						
	Right				0	1	2
	Left				0	1	2
14	Finger-Thumb Opposition						
	Right				0	1	2
	Left				0	1	2

15	Mirror Movements					
	Right			0	1	2
	Left			0	1	2
16	Finger - Nose Test					
	Right			0	1	2
	Left			0	1	2
17	Tandem walk			0	1	2
18	Romberg's			0	1	2
19	Adventitious Overflow					
	Right			0	1	2
	Left			0	1	2
20	Tremor					
	Right			0	1	2
	Left			0	1	2
21	Fist - ring test					
	Right			0	1	2
	Left			0	1	2
22	Fist - Edge - Palm test					
	Right			0	1	2
	Left			0	1	2
23	Ozeretski test			0	1	2
24	Audio visual Integration			0	1	2
25	Rhythm tapping test A (Reproduction)			0	1	2
26	Rhythm tapping test B (Production)			0	1	2

Name Age/Sex OP No.

POSITIVE AND NEGATIVE SYNDROME SCALE				
POSITIVE SCALE (P)				
P1. Delusions				
P2. Conceptual disorganization				
P3. Hallucinatory behavior				
P4. Excitement				
P5. Grandiosity				
P6. Suspiciousness/persecution				
P7. Hostility				
NEGATIVE SCALE (N)				
N1. Blunted affect				
N2. Emotional withdrawal				
N3. Poor rapport				
N4. Passive/apathetic social withdrawal				
N5. Difficulty in abstract thinking				
N6. Lack of spontaneity and flow of conversation				
N7. Stereotyped thinking				
GENERAL PSYCHOPATHOLOGY SCALE (G)				
G1. Somatic concern				
G2. Anxiety				
G3. Guiltfeelings				
G4. Tension				
G5. Mannerisms and posturing				
G6. Depression				
G7. Motor retardation				
G8. Uncooperativeness				
G9. Unusual thought content				
G10. Disorientation				
G11. Poor attention				
G12. Lack of judgment and insight				
G13. Disturbance of volition				
G14. Poor impulse control				
G15. Preoccupation				
G16. Active social avoidance				

ANNEXURE - I

ICD – 10 DIAGNOSTIC CRITERIA FOR RESEARCH

CRITERIA FOR DIAGNOSIS OF SCHIZOPHRENIA

F20 SCHIZOPHRENIA

This overall category includes the common varieties of schizophrenia, together with some less common varieties and closely related disorders.

F20.0 - F20.3

General criteria for Paranoid, Hebephrenic, Catatonic and Undifferentiated type of Schizophrenia:

G1. Either at least one of the syndromes, symptoms and signs listed below under (1), or at least two of the symptoms and signs listed under (2), should be present for most of the time during an episode of psychotic illness lasting for at least one month (or at some time during most of the days).

(1) At least one of the following:

(a) Thought echo, thought insertion or withdrawal, or thought broadcasting.

(b) Delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception.

(c) Hallucinatory voices giving a running commentary on the patient's behaviour, or discussing him between themselves, or other types of hallucinatory voices coming from some part of the body.

(d) Persistent delusions of other kinds that are culturally inappropriate and completely impossible (e.g. being able to control the weather, or being in communication with aliens from another world).

(2) or at least two of the following:

(a) e) Persistent hallucinations in any modality, when occurring every day for at least one month, when accompanied by delusions (which may be fleeting or half-formed) without clear affective content, or when accompanied by persistent over-valued ideas.

(e) f) Neologisms, breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech.

(f) g) Catatonic behaviour, such as excitement, posturing or waxy flexibility, negativism, mutism and stupor.

(g) h) "Negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses (it must be clear that these are not due to depression or to neuroleptic medication).

G2. Most commonly used exclusion criteria: If the patient also meets criteria for manic episode (F30) or depressive episode (F32), the criteria listed under G1.1 and

G1.2 above must have been met before the disturbance of mood developed.

G3. The disorder is not attributable to organic brain disease (in the sense of F0), or to alcohol- or drug-related intoxication, dependence or withdrawal.

Comments: In evaluating the presence of these abnormal subjective experiences and behaviour, special care should be taken to avoid false-positive assessments, especially where culturally or sub-culturally influenced modes of expression and behaviour, or a subnormal level of intelligence, are involved.

In view of the considerable variation of the course of schizophrenic disorders it may be desirable (especially for research) to specify the pattern of course by using a

fifth character. Course should not usually be coded unless there has been a period of observation of at least one year

Pattern of course

F20.x0 Continuous (no remission of psychotic symptoms throughout the period of observation);

F20.x1 Episodic, with a progressive development of 'negative' symptoms in the intervals between psychotic episodes;

F20.x2 Episodic, with persistent but non-progressive 'negative' symptoms in the intervals between psychotic episodes;

F20.x3 Episodic (remittent) with complete or virtually complete remissions between psychotic episodes;

F20.x4 Incomplete remission;

F20.x5 Complete or virtually complete remission;

F20.x8 Other pattern of course.

F20.x9 Course uncertain, period of observation too short.

F20.0 Paranoid schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3 above) must be met.

B. Delusions or hallucinations must be prominent (such as delusions of persecution, reference, exalted birth, special mission, bodily change or jealousy; threatening or commanding voices, hallucinations of smell or taste, sexual or other bodily sensations).

C. Flattening or incongruity of affect, catatonic symptoms, or incoherent speech must not dominate the clinical picture, although they may be present to a mild degree.

F20.1 Hebephrenic schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3) above must be met.

B. Either (1) or (2):

(1) Definite and sustained flattening or shallowness of affect;

(2) Definite and sustained incongruity or inappropriateness of affect.

C. Either (1) or (2):

(1) Behaviour which is aimless and disjointed rather than goal-directed;

(2) Definite thought disorder, manifesting as speech which is disjointed, rambling or incoherent.

D. Hallucinations or delusions must not dominate the clinical picture, although they may be present to a mild degree.

F20.2 Catatonic schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3 above) must eventually be met, though this may not be possible initially if the patient is uncommunicative.

B. For a period of at least two weeks one or more of the following catatonic behaviours must be prominent:

(1) Stupor (marked decrease in reactivity to the environment and reduction of spontaneous movements and activity) or mutism;

(2) Excitement (apparently purposeless motor activity, not influenced by external stimuli);

(3) Posturing (voluntary assumption and maintenance of inappropriate or bizarre postures);

(4) Negativism (an apparently motiveless resistance to all instructions or attempts to be moved, or movement in the opposite direction);

(5) Rigidity (maintenance of a rigid posture against efforts to be moved);

(6) Waxy flexibility (maintenance of limbs and body in externally imposed positions);

(7) Command automatism (automatic compliance with instructions).

C. Other possible precipitants of catatonic behaviour, including brain disease and metabolic disturbances, have been excluded.

F20.3 Undifferentiated schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3) above must be met.

B. Either (1) or (2):

(1) There are insufficient symptoms to meet the criteria of any of the sub-types F20.0, .1, .4, or .5;

(2) There are so many symptoms that the criteria for more than one of the subtypes listed in B (1) above are met.

F20.4 Post-schizophrenic depression

A. The general criteria for schizophrenia (F20.0 - F20.3 above) must have been met within the past twelvemonths, but are not met at the present time.

B. One of F20 G1.2 e, f, g or h must still be present.

C. The depressive symptoms must be sufficiently prolonged, severe and extensive to meet criteria for at least a mild depressive episode (F32.0).

F20.5 Residual schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3 above) must have been met at some time in the past, but are not met at the present time.

B. At least four of the following 'negative' symptoms have been present throughout the previous twelvemonths:

(1) Psychomotor slowing or under activity;

(2) Definite blunting of affect;

(3) Passivity and lack of initiative;

(4) Poverty of either the quantity or the content of speech;

(5) Poor non-verbal communication by facial expression, eye contact, voice modulation or posture;

(6) Poor social performance or self-care.

F20.6 Simple schizophrenia

A. Slowly progressive development over a period of at least one year, of all three of the following:

(1) A significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of drive and interests, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.

(2) Gradual appearance and deepening of "negative" symptoms such as marked apathy, paucity of speech, under activity, blunting of affect, passivity and lack of initiative, and poor non-verbal communication (by facial expression, eye contact, voice modulation and posture).

(3) Marked decline in social, scholastic, or occupational performance.

B. Absence, at any time, of any symptoms referred to in G1 in F20.0 - F20.3, and of hallucinations or well-formed delusions of any kind, i.e. the subject must never have met the criteria for any other type of schizophrenia, or any other psychotic disorder.

C. Absence of evidence of dementia or any other organic mental disorder listed in section F0.

F20.8 Other schizophrenia

F20.9 Schizophrenia, unspecified

ANNEXURE - II

POSITIVE AND NEGATIVE SYNDROME SCALE (PANSS)

No. Item Score

POSITIVE SCALE

P1 Delusions

Beliefs which are unfounded, unrealistic and idiosyncratic.

Basis for rating: Thought content expressed in the interview and its influence on social relations and behaviour

P2 Conceptual disorganisation

Disorganised process of thinking characterized by disruption of goal-directed sequencing, e.g. Circumstantiality, tangentiality, loose associations on sequiturs, gross illogicality, or thought block.

Basis for rating: cognitive-verbal processes observed during the course of interview.

P3 Hallucinatory behaviour

Verbal report or behaviour indicating perceptions which are not generated by external stimuli. These may occur in the auditory visual, olfactory, or somatic realms.

Basis for rating: verbal report and physical manifestations during the course of interview as well as reports of behaviour by primary care workers or family.

P4 Hyperactivity as reflected in accelerated motor behaviour, heightened responsivity to stimuli hypervigilance, or excessive mood lability.

Basis for rating: behavioural manifestations during the course of interview as well as reports of behaviour by primary care workers or family.

P5 Grandiosity

Exaggerated self-opinion and unrealistic convictions of superiority, including delusions of extraordinary abilities, wealth,

knowledge, fame, power, and moral righteousness.

Basis for rating thought content expressed in the interview and its influence on behaviour.

P6 Suspiciousness/Persecution

Unrealistic or exaggerated ideas of persecution, as reflected in guardedness, a distrustful attitude, suspicious hypervigilance, or frank delusions that others mean one harm.

Basis for rating: thought content expressed in the interview and its influence on behaviour.

P7 Hostility

Verbal and nonverbal expressions of range of anger and resentment, including sarcasm, passive-aggressive behaviour, verbal abuse, and assaultiveness.

Basis for rating: interpersonal behaviour observed during the interview and reports by primary care workers or family.

NEGATIVE SCALE

N1 Blunted affect

Diminished emotional responsiveness as characterized by a reduction in facial expression, modulation of feelings, and communicative gestures.

Basis for rating: observation of physical manifestations of affective tone and emotional responsiveness during the course of interview.

N2 Emotional withdrawal

Lack of interest in, involvement with, and affective commitment to life's events.

Basis for rating: reports of functioning form primary care workers or family and observation of interpersonal behaviour during the course of interview.

N3 Lack of interpersonal empathy, openness in conversation, and sense of closeness, interest, or involvement with the interviewer. This is evidenced by interpersonal distancing and reduced verbal and nonverbal communication.

Basis for rating: interpersonal behaviour during the course of interview.

N4 Passive/apathetic social withdrawal

Diminished interest and initiative in social interactions due to passivity, apathy, anergy, or avolition. This leads to reduced interpersonal involvement and neglect of activities of daily living.

Basis for rating: reports on social behaviour from primary care workers or family.

N5 Difficulty in abstract thinking

Impairment in the use of the abstract-symbolic mode of thinking, as evidenced by difficulty in classification, forming generalization, and proceeding beyond concrete or egocentric thinking in problem solving tasks.

Basis for rating: responses to questions on similarities and proverb interpretation, and use of concrete vs. Abstract mode during the course of the interview.

N6 Lack of spontaneity and flow of conversation

Reduction in the normal flow of communication associated with apathy, avolition, defensiveness, or cognitive deficit. This is manifested by diminished fluidity and productivity of the verbal-interpersonal process.

Basis for rating: cognitive-verbal processes observed during the course of interview.

N7 Stereotyped thinking

Decreased fluidity, spontaneity, and flexibility of thinking, as evidenced by in rigid, repetitious, or barren thought content.

Basis for rating: cognitive-verbal process observed during the interview.

GENERAL PSYCHOPATHOLOGY SCALE

G1 Somatic concern

Physical complaints or beliefs about bodily illness or malfunctions. This may range from a vague sense off ill being to clear-cut delusions of catastrophic physical disease.

Basis for rating: thought content expressed in the interview.

G2 Anxiety

Subjective experience of nervousness, worry, apprehension, or restlessness, ranging from excessive concern about the present or future to feelings of panic.

Basis for rating: verbal report during the course of interview and corresponding physical manifestations.

G3 Guilt feelings

Sense of remorse or self-blame for real or imagined misdeeds in the past.

Basis for rating: verbal report of guilt feelings during the course if interview and the influence on attitudes and thoughts.

G4 Tension

Overt physical manifestations of fear, anxiety, and agitation, such as stiffness, tremor, profuse sweating, and restlessness.

Basis for rating: verbal report attesting to anxiety and thereupon, the severity of physical manifestations of tension observed during the interview.

G5 Mannerisms and posturing

Unnatural movements or posture as characterized by an awkward, stilted, disorganized, or bizarre appearance.

Basis for rating: observation of physical manifestations during the course of interview as well as reports from primary care workers or family.

G6 Depression

Feelings of sadness, discouragement, helplessness and pessimism.

Basis for rating: verbal report of depressed mood during the course of interview and its observed influence on attitude and behaviour.

G7 Motor retardation

Reduction in motor activity as reflected in slowing or lessening of movements and speech, diminished responsiveness to stimuli, and reduced body tone.

Basis for rating: manifestations during the course of interview as well as reports by primary care workers or family.

G8 Uncooperativeness

Active refusal to company with the will of significant others, including the interviewer, hospital staff, or family, which may be associated with distrust, defensiveness, stubbornness, negativism, rejection of authority, hostility, or belligerence.

Basis for rating: interpersonal behaviour observed during the course of interview as well as reports from primary care workers or family.

G9 Unusual thought content

Thinking characterized by strange, fantastic, or bizarre ideas, ranging from those which are remote or atypical to those which are distorted, illogical, and patently absurd.

Basis for rating: thought content expressed during the course of interview.

G10 Disorientation

Lack of awareness of one's relationship to the milieu, including persons, place, and time, which may be due to confusion or withdrawal.

Basis for rating: responses to interview questions on orientation.

G11 Poor attention

Failure in focused alertness manifested by poor concentration, distractibility from internal and external stimuli, and difficulty in harnessing, sustaining, or shifting focus to new stimuli.

Basis for rating: manifestations observed during the course of interview.

G12 Lack of judgement and insight

Impaired awareness or understanding of one's own psychiatric condition and life situation. This is evidenced by failure to recognize psychiatric illness or symptoms, denial of need for psychiatric hospitalization or treatment, decisions characterized by poor anticipation of consequences, and unrealistic short-term

and long-range planning.

Basis for rating: thought content expressed during the interview.

G13 Disturbance of volition

Disturbance in the wilful initiation, sustenance, and control of one's thoughts, behaviour, movements, and speech.

Basis for rating: thought content and behaviour manifested in the course of interview.

G14 Poor impulse control

Disordered regulation and control of action on inner urges, resulting in sudden, unmodulated, arbitrary, misdirected discharge of tension and emotions, without concern about consequences.

Basis for rating: behaviour during the course of the interview and reported by primary care workers or family members.

G15 Preoccupation

Absorption with internally generated thoughts and feelings and with autistic experiences to the detriment of reality orientation and adaptive behaviour.

Basis for rating: interpersonal behaviour observed during the course of the interview.

G16 Active social avoidance

Diminished social involvement associated with unwarranted fear, hostility, or distrust. Basis for rating: reports of social functioning by primary care workers or family.

ANNEXURE - III

NEUROLOGICAL EVALUATION SCALE INSTRUCTIONS

1. Tandem walk: Instructions- subject to walk, in a straight line, 12 feet, heel to toe.

2. Romberg test:

3. Adventitious overflow:

4. Tremor: Instructions for test 2, 3, and 4: Subject to stand with feet together, eyes closed, arms held parallel to the floor, palms down, and fingers spread apart. The subject is to maintain this position for one minute.

5. Cerebral dominance/handedness: Ask subject to demonstrate how he/she would 1) write, 2) throw a ball, 3) use a tennis racket, 4) strike a match, 5) use scissors, 6) thread a needle, 7) use a broom, 8) use a shovel, 9) deal cards, 10) use a hammer, 11) brush teeth, and 12) unscrew the lid of a jar.

6. Cerebral dominance/footedness: Ask subject to demonstrate how he/she would kick a ball.

7. Cerebral dominance/eyedness: Ask subject, with both eyes open, to look at a distant object through a hole in the centre of a 3"x 5" index card that is held with both hands 18 inches in front of the subject. The subject is to close one eye at a time and tell the examiner with which eye closed did he/she lose sight of the object.

8. Audio-Visual Integration: The subject is asked to match a set of tapping sounds with one of the three sets of dots presented on a 3"x 5" index card. The

subject is instructed to close his/her eyes during the tapping. Three practice trials are performed first to ensure that the subject understands the directions. Ten trials.

9. Stereognosis: Subject, with eyes closed, is asked to identify an object placed in hand. Subject is instructed to feel the object with the one hand using thumb and forefinger and to take as much time as needed. If subject cannot name the object, he/she is asked to describe for what purpose the object is used. Start with right hand. The instructions are repeated at the beginning of the second trial.

10. Graphaesthesia: Subject with eyes closed, is asked to identify the number written on the tip of the forefinger with a pencil right hand first. Five trials for each hand.

11. Fist-Ring Test: The subject is asked to alternate placing hand on the table, in the position for a fist, with the thumb placed either over the knuckles or over the middle phalanges and placing hand, on the table, in the position of a ring, with the tips of the thumb and forefinger touching and the remaining three fingers extended. The subject is to bring arm into the upright position between each change in hand position. If the subject does not perform the movement accurately or in a manner that can be appropriately assessed initially, the test is to stop, re-instruct the subject, and start the test again. The subject is to repeat each set of hand position changes 15 times with each hand. Start with right hand.

12. Fist-Edge-Palm Test: Ask the subject, using a smooth and steady rhythmic pattern, to touch the table with the side of fist, edge of hand, and palm of hand.

The subject is to break contact with the surface of the table between each change in hand position, but not to bring the arm back in full flexion. The subject is to repeat this sequence of position changes 15 times. Start with right hand.

13. OzeretskiTest : The subject is to place both hands on the table, one hand palm down and the other hand in the shape of a fist. The subject is then asked simultaneously to alternate the position of the hands in a smooth and steady motion. The subject is asked to this motion 15times.

14. Memory: Subject is told four words (brown, honesty, tulip, eye dropper) and is asked to repeat them immediately after they are all presented. If the subject is unable to repeat the four words correctly, they are represented. If the subject cannot still repeat the four words after three presentations of the words, the test is terminated and the subjects is given a score of 2 for both parts of the item. If the subject is able to repeat the four words after the initial or two subsequent presentation, he/she is then asked to remember the words as well as possible and told that he/she will be asked to repeat the words twice later on during the interview. The subject is then asked to recall the four words at 5 and 10 minutes.

15. Rhythm Tapping Reproduction: In reproduction, ask the subject to reproduce exactly the series of taps heard while the subject has eyes closed. The subject may have his/her eyes open while reproducing series of taps. Strong and weak task are given in different sequences.

16. Rhythm Tapping Production: Ask the subject to produce the following series of taps: a series of two taps, a series of three taps, two strong taps and three weak taps, three weak taps and two strong taps, a series of three taps.

17. Rapid Alternating movements: Ask the subject to place hands palm down on legs. The subject is to start with right hand and is to slap leg distinctly with the palm and the back of the hand in an alternating motion. The subject is to perform the task 20times, with each hand.

18. Finger Thumb Opposition:

19. Mirror Movements: For items 18 and 19, ask the subject to place both hands palm up with fingers fully extended on legs. The subject is to start with right hand and is to touch the tip of fingers with the tip of thumb, from forefinger to pinky, returning to forefinger, for at least ten repetitions. The hand, which is not performing the Finger-Thumb Opposition Test, is observed for parallel movements of the fingers and thumb. When subject is using right hand, score mirror movements for right hand.

20. Extinction (Face-hand) Test: Subject is seated, with hands resting palm down, on his/her knees and with eyes closed. The subject is told that he/she will be touched on either the cheek, hand, or both, and is to say where he/she has been touched. If the subject names just one touch, he/she is asked–the first time this occurs only-if he/she felt a touch anywhere else. The simultaneous touching is done in the following order: right cheek- left hand, left cheek- right hand, right cheek- right hand, left cheek- left hand, both hands, and both cheeks. If touch is not reported, circle neglected location.

21. Right Left Confusion: Subject is asked to point to right foot, left hand, place right hand to left shoulder, left hand to right ear, point to examiner's left knee, right elbow, with examiner's arms crossed, point to examiner's left hand with his/her right hand, and with examiner re-crossing arms, point to examiner/right hand with his/her left hand.

22. Synkinesis: Subject is instructed to follow the cap of a pen with his/her eyes only as it is moved between extremes of horizontal haze, first from subject' right to left, then from subject's left to right. If the subject moves the eyes is asked to keep still and follow the cap with the eyes only.

23. Convergence: Subject is instructed to follow the cap of a pen with eyes as it is moved towards the subject's nose.

24. Gaze Impersistence: Subject is instructed to fix gaze without moving head on the cap of pen at a 45 degree angle in the horizontal plane of the right and left visual fields for 30 seconds.

25. Finger to Nose Test: The subject is instructed to close eyes and touch the very tip of your nose with the tip of your finger. First with the right finger. Then left.

26. Glabellar Reflex: Subject is instructed to fix gaze on a point across the room. The subject is approached from above the forehead (outside of the visual field), and the examiner taps the glabellar region ten times with the index finger.

27. Snout Reflex: Subject is instructed to relax, and the examiner presses finger against the subject's philtrum.

28. Grasp Reflex: The subject is instructed not to grab and examiner strokes the inside of subject's palm. This procedure is repeated a second time with the subject being asked to spell the word "help" backwards.

29. Suck Reflex: the examiner places the knuckle of a flexed index finger or tongue depressor between the subject's lips.

30. Palmomental Reflex: subject is instructed to extend hand, examiner scratches palm maximum six times beginning with right hand and then left.

ategory	Sl No	Age	Sex	Occu	Edn	Mar stat	SE Stat	Illness dur	Fam His	Posi score	Nega score	Handedness	AV integ	Stero L	Ster R	Graph R	Graph L	Extinc	R&L confu	Sens integr	Tandom	Rapid R	Rapid L	Fing thumb R	Finger thumb L	Fing nose R	Fing nose L	Motor Coord	First ring R	First ring L	First palm R	First palm L	Ozer test	Rhytm Tap	Seq com motor	Synken R	Synken L	Converge R	Conver L	Gaze R	Gaze L	Glapper	Grasp R	Grasp L	Snout ref	Suck ref	Mirror Move R	Mirror Move L	Romberge	Adventiou R	Advent L	Tremer R	Tremer L	Production	Mem 10 Minu	Mem 5 Minu	Others	Grand Total
N	1	38	2	3	9	2	1	2	2	12	24	1	2	0	0	0	2	1	0	5	0	0	0	1	1	0	0	2	1	2	1	1	2	2	9	2	2	2	2	2	2	2	1	1	2	0	0	0	0	0	1	0	0	0	1	1	20	36
N	2	36	2	2	5	1	1	6	1	14	28	1	2	1	1	2	2	1	2	11	2	0	0	2	2	0	0	6	1	1	1	1	2	2	8	2	2	2	2	2	2	2	0	0	0	0	2	2	0	0	0	0	0	2	2	2	24	49
N	3	21	2	2	9	2	1	2	1	11	25	1	2	0	0	1	1	0	0	4	0	0	0	0	0	0	0	0	0	0	2	2	2	2	8	0	0	1	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	2	2	1	9	21
N	4	20	2	1	6	1	1	1	3	12	34	1	2	0	0	2	2	0	2	8	2	2	2	2	2	1	1	12	2	2	2	2	2	2	12	2	2	2	2	2	2	0	0	0	0	0	2	2	1	1	1	2	2	2	2	2	29	61
N	5	37	1	1	10	3	1	2	1	10	18	1	1	0	0	2	2	0	0	5	0	0	0	1	0	0	0	1	0	2	1	1	0	2	6	2	2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1	2	2	2	13	25
N	6	27	1	1	8	1	1	3	1	16	27	2	2	0	0	1	2	0	1	6	0	0	0	1	1	0	0	2	2	2	2	2	0	2	10	0	0	2	2	2	2	1	1	0	0	0	0	0	0	1	1	1	2	1	1	1	20	38
N	7	29	2	1	12	1	1	4	2	21	37	1	2	0	0	1	1	0	2	6	2	0	0	1	1	0	0	4	2	2	1	1	1	2	9	2	2	0	2	2	2	2	1	1	2	0	0	0	2	1	1	1	1	1	2	2	26	45
N	8	40	1	1	12	3	1	3	1	13	32	1	2	0	0	0	0	0	0	6	0	1	1	1	1	0	0	4	1	1	1	1	1	2	10	1	1	2	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	26	46
N	8	21	2	1	9	1	1	3	1	18	35	2	2	0	0	1	2	0	1	2	2	0	0	0	0	1	1	4	1	1	2	2	2	2	7	1	1	1	1	1	1	1	2	2	0	0	0	0	2	2	2	2	2	2	2	1	13	26
N	10	27	2	2	10	2	1	5	3	14	36	1	1	0	0	2	2	0	1	6	1	0	0	0	0	0	0	1	0	0	1	2	0	1	4	1	1	2	2	1	1	2	0	0	0	0	1	1	0	0	0	1	1	0	0	0	14	25
N	11	50	2	1	5	3	1	5	1	17	32	1	2	2	2	2	2	0	2	12	2	2	2	2	2	2	2	14	2	2	2	2	2	2	12	2	2	2	2	2	2	2	0	0	0	0	0	0	0	2	2	1	1	2	2	2	26	64
N	12	34	1	3	10	1	2	5	1	12	40	1	2	0	0	2	0	0	2	6	0	1	1	0	0	0	0	2	1	0	0	0	0	2	3	2	2	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	1	0	0	0	8	19
N	13	33	1	3	7	1	1	2	1	11	23	1	2	0	0	2	2	2	2	10	1	0	0	1	1	1	0	4	0	0	2	2	2	2	8	1	1	1	1	0	0	2	0	0	0	0	0	0	0	0	0	1	0	2	2	2	13	35
N	14	25	1	3	12	1	1	5	1	14	39	1	2	1	1	2	2	0	1	9	1	2	2	2	2	1	1	11	2	2	2	2	0	2	10	2	2	2	2	2	2	2	0	0	0	0	2	2	0	0	0	1	1	2	2	2	26	56
N	15	27	1	1	5	2	1	3	1	23	40	2	2	1	2	2	2	0	2	11	0	2	2	2	2	0	0	8	2	2	2	2	0	2	10	2	2	2	2	2	2	2	1	1	0	2	1	0	0	1	1	2	2	2	2	2	31	60
N	16	26	1	1	15	1	2	2	2	13	40	1	1	0	0	2	2	0	0	5	0	0	0	0	0	1	1	0	0	0	1	1	0	0	2	2	2	1	1	0	0	2	0	0	0	0	0	0	1	0	1	1	0	1	1	1	13	21
N	17	43	1	3	5	3	1	5	1	21	32	1	2	1	1	2	2	0	1	9	1	2	2	2	2	1	1	11	2	2	2	2	0	2	10	2	2	2	2	2	2	2	0	0	0	0	2	2	0	0	1	1	2	1	1	1	24	54
N	18	25	1	1	6	1	1	3	2	40	14	1	2	0	0	2	1	0	2	7	0	1	1	0	0	0	0	2	1	0	0	0	0	2	3	2	2	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	1	0	0	0	8	20
N	19	27	2	1	13	2	2	2	1	18	34	2	2	1	0	2	2	0	2	11	0	2	2	2	2	0	0	8	2	2	2	2	0	2	10	2	2	2	2	2	2	2	1	1	0	2	1	0	0	1	1	2	2	2	2	2	31	60
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N	21	24	1	3	9	1	1	2	2	32	16	1	2	0	0	1	1	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	7
N	22	23	1	1	12	1	1	4	2	14	32	2	2	0	0	1	2	0	1	6	0	0	0	1	1	0	0	2	2	2	2	2	0	2	10	0	0	2	2	2	2	1	1	0	0	0	0	0	0	1	1	1	1	2	1	1	20	38
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P	1	24	2	2	5	2	1	1	2	32	25	1	2	0	0	1	1	0	1	5	0	0	0	1	1	0	0	2	2	2	2	2	2	2	12	2	2	2	2	2	2	1	0	0	0	0	0	0	0	0	0	1	1	2	2	2	21	40
P	2	24	1	1	15	1	2	1	1	33	19	1	2	0	0	1	0	0	1	4	0	0	0	0	0	0	0	0	1	1	0	0	0	2	4	2	2	2	2	2	2	2	1	0	0	0	0	0	0	0	0	0	2	0	0	0	19	27
P	3	35	2	2	12	2	1	6	1	36	16	1	1	0	0	2	2	0	0	5	1	0	1	0	0	0	0	2	1	1	1	1	0	1	5	0	0	1	1	1	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	6	18
P	4	40	2	2	5	2	1	4	1	34	13	1	1	0	0	2	2	0	0	5	0	0	0	1	1	0	0	2	2	2	2	2	2	2	12	1	1	1	1	1	1	1	1	0	1	1	1	1	0	0	0	1	1	1	2	2	19	38
P	5	32	2	2	7	3	1	1	1	30	16	1	2	0	0	2	2	0	0	6	1	1	0	0	0	1	2	5	2	2	2	2	0	2	10	1	1	1	1	2	2	2	1	1	2	1	0	0	1	1	1	1	2	2	2	2	27	48
P	6	24	2	4	12	1	1	1	3	25	12	1	2	0	0	1	1	0	0	4	0	0	0	0	0	0	0	0	2	2	2	2	0	1	9	1	1	1	1	2	2	1	0	0	0	0	0	0	1	1	1	1	1	2	1	17	30
P	7	38	1	3	12	2	1	5	1	22	17	1	2	0	0	0	0	0	0	2	0	0	0	0	0	0	0	3	0	0	1	1	0	2	4	0	0	0	0	0	1	1	0	0	1	1	0	0	0	0	0	0	0	1	0	0	11	20
P	8	38	2	2	8	2	1	2	1	32	16	1	2	0	0	1	1	0	0	2	0	0	1	0	0	0	0	3	0	0	0	0	0	2	4	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11	20
P	9	35	2	2	5	2	1	4	1	32	22	1	2	1	1	2	2	1	1	4	1	2	2	1	1	0	0	1	2	2	2	2	2	2	2	2	2	2	2	2	2	1	0	0	0	0	0	0	0	0	0	0	2	2	2	1	8
P	10	45	2	2	5	2	1	0	1	30	16	1	2	0	0	2	2	0	1	10	2	1	1	1	1	1	1	7	2	2	1	1	1	2	12	1	1	1	1	1	1	2	0	1	0	0	0	0	1	1	1	1	1	1	1	1	19	48
P	11	25	1	3	6	1	1	1	1	32	12	1	2	0	0	1	1	0	1	7	0	2	2	0	0	0	0	8	2	2	2	2	0	2	9	1	1	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	2	2	2	17	41
P	12	23	1	1	9	1	1	1	1	40	14	2	2	0	0	2	2	0	0	5	0	1	1	1	1	0	0	4	0	0	1	0	0	2	12	0	0	1	1	2	2	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	11	32
P	13	38	2	2	12	2	1	2	2	30	15	1	2	0	0	2	2	0	1	6	1	0	0	1	1	0	0	4	1	1	0	0	2	2	3	0	0	1	1	1	1	1	0	0	0	0	0	0	1	1	1	1	1	1	2	2	9	22
P	14	23	2	2	5	3	1	1	2	25	10	1	2	0	0	1	1	0	0	6	1	0	0	0	1	1	1	4	1	1	2	1	2	2	3	1	1	1	1	0	0	2	1	1	2	0	0	0	1	1	1	1	1	2	1	1	9	22
P	15	48	1	3	7	2	1	2	1	32	12	1	1	0	0	2	2	0	0	7	1	0	1	0	0	0	0	3	1	1	1	1	0	1	6	0	0	1	1	1	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	15	31
P	16	31	2	2	16	2	2	1	1	38	14	2	2	0	0	0	0	0	0	4	0	1	1	1	1	0	0	4	0	0	1	0	0	2	9	0	0	1	1	2	2	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	19	36
P	17	30	2	2	9	2	1	2	2	38	14	1	2	0	0	2	1	0	0	5	0	0	0	0	0	1	1	2	0	0	0	0	0	2	5	1	1	1	1	1	1	0	1	1	0	0	0	0	1	1	1	1	1	2	0	0	6	18

P	18	21	1	3	13	1	1	2	3	26	12	1	2	0	0	1	1	0	1	2	0	2	2	0	0	0	0	4	2	2	2	2	2	2	3	1	1	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	2	2	2	9	18
P	19	55	2	1	5	3	1	3	1	26	14	1	2	0	0	2	2	0	0	5	0	1	1	1	1	0	0	2	0	0	1	0	0	2	2	0	0	1	1	2	2	0	0	0	0	0	0	0	1	0	0	0	0	0	2	2	15	24
P	20	26	2	1	12	1	1	2	1	26	16	1	1	1	1	0	2	1	1	5	1	0	0	1	1	1	1	4	1	1	1	1	0	1	12	2	2	1	1	2	1	1	1	1	0	0	0	0	1	0	0	1	1	0	2	1	11	32
P	21	25	2	2	5	2	1	0	1	40	12	1	2	0	0	2	2	0	1	7	1	0	0	1	1	0	0	5	1	1	0	0	2	2	5	0	0	1	1	1	1	1	0	0	0	0	0	0	1	1	1	1	1	2	2	2	18	35
P	22	35	2	2	12	2	1	6	1	36	16	1	1	0	0	2	2	0	0	7	1	0	1	0	0	0	0	3	1	1	1	1	0	1	6	0	0	1	1	1	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	16	32
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P	24	32	2	2	7	3	1	1	1	30	16	1	2	0	0	2	2	0	0	5	1	1	0	0	0	1	2	2	2	2	2	2	0	2	12	1	1	1	1	2	2	2	1	1	2	1	0	0	1	1	1	1	2	2	2	2	19	38
P	25	31	2	2	16	2	2	1	1	38	14	2	2	0	0	0	0	0	0	6	0	1	1	1	1	0	0	5	0	0	1	0	0	2	10	0	0	1	1	2	2	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	27	48
P	26	30	2	2	9	2	1	2	2	38	14	1	2	0	0	2	1	0	0	2	0	0	0	0	0	1	1	4	0	0	0	0	0	2	3	1	1	1	1	1	1	0	1	1	0	0	0	0	1	1	1	1	1	2	0	0	9	18
P	27	21	1	3	13	1	1	2	3	26	12	1	2	0	0	1	1	0	1	5	0	2	2	0	0	0	0	2	2	2	2	2	2	2	2	1	1	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	2	2	2	15	24
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